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☐	L9	L8 and N-terminus	21
☐	L8	L7 and albumin	41
☐	L7	bar-or	136
	DB=USPT; PLUR=YES; OP=OR		
☐	L6	6767708	1
☐	L5	5326707	4
☐	L4	L3 and fleer	10
☐	L3	5876969	28
☐	L2	6235489	2
☐	L1	6274305	1

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☐ 1. Document ID: US 20050142613 A1

L9: Entry 1 of 21 File: PGPB Jun 30, 2005

PGPUB-DOCUMENT-NUMBER: 20050142613
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20050142613 A1

TITLE: Test for the rapid evaluation of ischemic states and kits

PUBLICATION-DATE: June 30, 2005

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Bar-Or, David	Englewood	CO	US	
Lau, Edward	Boulder	CO	US	
Winkler, James V.	Denver	CO	US	
Fagan, Gary	Broomfield	CO	US	
Wayment, Hollie	Elizabeth	CO	US	

US-CL-CURRENT: 435/7.1; 530/363

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

☐ 2. Document ID: US 20050021235 A1

L9: Entry 2 of 21 File: PGPB Jan 27, 2005

PGPUB-DOCUMENT-NUMBER: 20050021235
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20050021235 A1

TITLE: Method and system for optically performing an assay to determine a medical condition

PUBLICATION-DATE: January 27, 2005

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Bar-Or, Raphael	Denver	CO	US	
Bar-Or, David	Englewood	CO	US	
Curtis, C. Gerald	Penylan Cardiff		GB	

US-CL-CURRENT: 702/19

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

☐ 3. Document ID: US 20040209379 A1

L9: Entry 3 of 21 File: PGPB Oct 21, 2004

PGPUB-DOCUMENT-NUMBER: 20040209379
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20040209379 A1

TITLE: Diagnosis and monitoring of diseases

PUBLICATION-DATE: October 21, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Bar-Or, David	Englewood	CO	US	
Bar-Or, Raphael	Denver	CO	US	

US-CL-CURRENT: 436/86

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

☐ 4. Document ID: US 20040175754 A1

L9: Entry 4 of 21 File: PGPB Sep 9, 2004

PGPUB-DOCUMENT-NUMBER: 20040175754
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20040175754 A1

TITLE: Diagnosis and monitoring of inflammation, ischemia and appendicitis

PUBLICATION-DATE: September 9, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Bar-Or, David	Englewood	CO	US	
Bar-Or, Raphael	Denver	CO	US	
Winkler, James V.	Denver	CO	US	
Yukl, Richard L.	Denver	CO	US	

US-CL-CURRENT: 435/7.1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

☐ 5. Document ID: US 20030215952 A1

L9: Entry 5 of 21 File: PGPB Nov 20, 2003

PGPUB-DOCUMENT-NUMBER: 20030215952
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20030215952 A1

TITLE: Tests for the rapid evaluation of ischemic states and kits

PUBLICATION-DATE: November 20, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Bar-Or, David	Englewood	CO	US	
Lau, Edward	Boulder	CO	US	
Winkler, James V.	Denver	CO	US	

US-CL-CURRENT: 436/74; 530/363

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

☐ 6. Document ID: US 20030215359 A1

L9: Entry 6 of 21 File: PGPB Nov 20, 2003

PGPUB-DOCUMENT-NUMBER: 20030215359
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20030215359 A1

TITLE: Tests for the rapid evaluation of ischemic states and kits

PUBLICATION-DATE: November 20, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Bar-Or, David	Englewood	CO	US	
Lau, Edward	Boulder	CO	US	
Winkler, James V.	Denver	CO	US	

US-CL-CURRENT: 422/61

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

☐ 7. Document ID: US 20030194813 A1

L9: Entry 7 of 21 File: PGPB Oct 16, 2003

PGPUB-DOCUMENT-NUMBER: 20030194813
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20030194813 A1

TITLE: Tests for the rapid evaluation of ischemic states and kits

PUBLICATION-DATE: October 16, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Bar-Or, David	Englewood	CO	US	
Lau, Edward	Boulder	CO	US	
Winkler, James V.	Denver	CO	US	

US-CL-CURRENT: 436/74; 436/518

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

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☐ 8. Document ID: US 20030190691 A1

L9: Entry 8 of 21 File: PGPB Oct 9, 2003

PGPUB-DOCUMENT-NUMBER: 20030190691
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20030190691 A1

TITLE: Tests for the rapid evaluation of ischemic states and kits

PUBLICATION-DATE: October 9, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Bar-Or, David	Englewood	CO	US	
Lau, Edward	Boulder	CO	US	
Winkler, James V.	Denver	CO	US	

US-CL-CURRENT: 435/7.32

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

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☐ 9. Document ID: US 20030180820 A1

L9: Entry 9 of 21 File: PGPB Sep 25, 2003

PGPUB-DOCUMENT-NUMBER: 20030180820
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20030180820 A1

TITLE: Tests for the rapid evaluation of ischemic states and kits

PUBLICATION-DATE: September 25, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47

Bar-Or, David	Englewood	CO	US
Lau, Edward	Boulder	CO	US
Winkler, James V.	Denver	CO	US
Fagan, Gary	Broomfield	CO	US
Wayment, Hollie	Elizabeth	CO	US

US-CL-CURRENT: 435/7.32

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

☐ 10. Document ID: US 20030158111 A1

L9: Entry 10 of 21 File: PGPB Aug 21, 2003

PGPUB-DOCUMENT-NUMBER: 20030158111
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20030158111 A1

TITLE: Methods and products for oral care

PUBLICATION-DATE: August 21, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Bar-Or, David	Englewood	CO	US	

US-CL-CURRENT: 514/12; 424/50, 514/13, 514/14, 514/15, 514/16, 514/17, 514/18

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

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Search Results - Record(s) 11 through 20 of 21 returned.

☐ 11. Document ID: US 20030132125 A1

L9: Entry 11 of 21 File: PGPB Jul 17, 2003

PGPUB-DOCUMENT-NUMBER: 20030132125
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20030132125 A1

TITLE: Electrochemical detection of ischemia

PUBLICATION-DATE: July 17, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Wayment, Hollie	Elizabeth	CO	US	
Fagan, Gary	Broomfield	CO	US	
Crosby, Peter A.	Denver	CO	US	
George, Shannon	Westminster	CO	US	

US-CL-CURRENT: 205/792; 204/403.01

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

☐ 12. Document ID: US 20030130185 A1

L9: Entry 12 of 21 File: PGPB Jul 10, 2003

PGPUB-DOCUMENT-NUMBER: 20030130185
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20030130185 A1

TITLE: Metal-binding compounds and uses therefor

PUBLICATION-DATE: July 10, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Bar-Or, David	Englewood	CO	US	
Curtis, C. Gerald	Penylan	CO	GB	
Lau, Edward	Boulder	CO	US	
Rao, Nagaraja K.R.	Cardiff	CO	GB	
Winkler, James V.	Denver		US	

Crook, Wannell M. Castle Rock US

US-CL-CURRENT: 514/12; 514/16, 514/17, 514/18

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

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☐ 13. Document ID: US 20030060408 A1

L9: Entry 13 of 21 File: PGPB Mar 27, 2003

PGPUB-DOCUMENT-NUMBER: 20030060408
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20030060408 A1

TITLE: Metal-binding compounds and uses therefor

PUBLICATION-DATE: March 27, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Bar-Or, David	Englewood	CO	US	
Curtis, C. Gerald	Cardiff	CO	GB	
Lau, Edward	Boulder	CO	US	
Rao, Nagaraja K.R.	Cardiff	CO	GB	
Winkler, James V.	Denver		US	
Crook, Wannell M.	Castle Rock		US	

US-CL-CURRENT: 514/12; 530/324

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

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☐ 14. Document ID: US 20030055003 A1

L9: Entry 14 of 21 File: PGPB Mar 20, 2003

PGPUB-DOCUMENT-NUMBER: 20030055003
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20030055003 A1

TITLE: Use of copper chelators to inhibit the inactivation of protein C

PUBLICATION-DATE: March 20, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Bar-Or, David	Englewood	CO	US	
Yukl, Richard L.	Denver	CO	US	

US-CL-CURRENT: 514/18; 530/330, 530/331

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw. De

☐ 15. Document ID: US 20030044353 A1

L9: Entry 15 of 21 File: PGPB Mar 6, 2003

PGPUB-DOCUMENT-NUMBER: 20030044353
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20030044353 A1

TITLE: Activatable imaging probes

PUBLICATION-DATE: March 6, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Weissleder, Ralph	Charlestown	MA	US	
Tung, Ching-Hsuan	Wayland	MA	US	
Mahmood, Umar	Winchester	MA	US	

US-CL-CURRENT: 424/9.6; 424/178.1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw. De

☐ 16. Document ID: US 20030017506 A1

L9: Entry 16 of 21 File: PGPB Jan 23, 2003

PGPUB-DOCUMENT-NUMBER: 20030017506
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20030017506 A1

TITLE: Marker useful for detection and measurement of free radical damage and method

PUBLICATION-DATE: January 23, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Bar-Or, David	Englewood	CO	US	
Lau, Edward	Boulder	CO	US	

US-CL-CURRENT: 435/7.1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw. De

☐ 17. Document ID: US 6787636 B1

L9: Entry 17 of 21 File: USPT Sep 7, 2004

US-PAT-NO: 6787636
DOCUMENT-IDENTIFIER: US 6787636 B1

TITLE: Modified serum albumin with reduced affinity for nickel and copper

DATE-ISSUED: September 7, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Carter; Daniel C.	Madison	AL		

US-CL-CURRENT: 530/363; 435/252.3, 435/69.1, 435/69.6, 435/71.1, 530/324, 530/362

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw De

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☐ 18. Document ID: US 6492179 B1

L9: Entry 18 of 21 File: USPT Dec 10, 2002

US-PAT-NO: 6492179
DOCUMENT-IDENTIFIER: US 6492179 B1
**** See image for Certificate of Correction ****

TITLE: Test for rapid evaluation of ischemic states and kit

DATE-ISSUED: December 10, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Bar-Or; David	Englewood	CO		
Lau; Edward	Boulder	CO		
Winkler; James V.	Denver	CO		

US-CL-CURRENT: 436/74; 422/55, 422/56, 422/58, 422/66, 422/82.05, 422/82.09, 435/4, 435/7.1, 436/171, 436/518, 436/63, 436/73, 436/86, 436/87, 436/88, 436/903, 436/904

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw De

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☐ 19. Document ID: US 6475743 B1

L9: Entry 19 of 21 File: USPT Nov 5, 2002

US-PAT-NO: 6475743
DOCUMENT-IDENTIFIER: US 6475743 B1

TITLE: Marker useful for detection and measurement of free radical damage and method

DATE-ISSUED: November 5, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Bar-Or; David	Englewood	CO		
Lau; Edward	Boulder	CO		

US-CL-CURRENT: 435/7.1; 422/55, 422/56, 422/58, 422/66, 422/82.09, 435/4, 436/171, 436/518, 436/536, 436/63, 436/73, 436/74, 436/86, 436/88, 436/903, 436/904

Full | Title | Citation | Front | Review | Classification | Date | Reference | | | Claims | KWIC | Draw De

☐ 20. Document ID: US 6461875 B1

L9: Entry 20 of 21 File: USPT Oct 8, 2002

US-PAT-NO: 6461875
DOCUMENT-IDENTIFIER: US 6461875 B1

TITLE: Test for rapid evaluation of ischemic states and kit

DATE-ISSUED: October 8, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Bar-Or; David	Englewood	CO		
Lau; Edward	Boulder	CO		
Winkler; James V.	Denver	CO		

US-CL-CURRENT: 436/536; 422/82.05, 422/82.09, 435/4, 435/7.9, 436/518, 436/86

Full | Title | Citation | Front | Review | Classification | Date | Reference | | | Claims | KWIC | Draw De

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L9: Entry 16 of 21 File: PGPB Jan 23, 2003

PGPUB-DOCUMENT-NUMBER: 20030017506
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20030017506 A1

TITLE: Marker useful for detection and measurement of free radical damage and method

PUBLICATION-DATE: January 23, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Bar-Or, David	Englewood	CO	US	
Lau, Edward	Boulder	CO	US	

US-CL-CURRENT: 435/7.1

CLAIMS:

We claim:

1. A marker for the detection of free radical damage, comprising modified albumin, wherein said albumin is modified in a manner which results in inhibition of the metal binding capacity of the N-terminus of said albumin.

2. The marker of claim 1, wherein said albumin is human serum albumin.

3. A method for detecting and quantifying the presence of the marker of claim 1, comprising the steps of: (a) contacting a biological sample containing albumin with an excess quantity of a metal ion salt, said metal ion capable of binding to the N-terminus of naturally occurring human albumin, to form a mixture containing bound metal ions and unbound metal ions, (b) determining the amount of bound metal ions, and (c) correlating the amount of bound metal ions to a known value to determine the quantity of the marker present.

4. The method of claim 3, wherein said excess quantity of metal ion salt is a predetermined quantity and the quantity of unbound metal ions is detected to determine the amount of bound metal ions.

5. The method of claim 4, further comprising the step of: (a) adding the compound Asp-Ala-His-Lys-R, wherein R is a group capable of being detected when bound to said metal ion salt, to the mixture containing bound metal ions and unbound metal ions, (b) detecting the quantity of R to detect the quantity of unbound metal ions.

6. The method of claim 3, wherein said sample is serum or plasma.

7. The method of claim 3, wherein said sample is purified albumin.

8. The method of claim 3, wherein said metal ion salt is a salt of a transition metal ion of Groups 1b-7b or 8 of the Periodic Table of the elements.

9. The method of claim 3, wherein said metal ion salt is a salt of a metal selected from the group consisting of V, As, Co, Sb, Cr, Mo, Mn, Ba, Zn, Ni, Hg, Cd, Fe, Pb, Au and Ag.

10. The method of claim 3, wherein said metal ion is cobalt.

11. The method of claim 3, wherein step (b) is conducted using atomic absorption or atomic emission spectroscopy.

12. The method of claim 3, wherein step (b) is conducted using an immunological assay.

13. The method of claim 4, wherein detection of the quantity of unbound metal ions is conducted using atomic absorption or atomic emission spectroscopy.

14. The method of claim 4, wherein detection of the quantity of unbound metal ions is conducted using is conducted using an immunological assay.

15. The method of claim 5, wherein the determination of the quantity of said compound which is complexed with said metal ion salt is conducted using atomic absorption or atomic emission spectroscopy.

16. The method of claim 5, wherein the determination of the quantity of said compound which is complexed with said metal ion salt is conducted using an immunological assay.

17. A method for detecting and quantifying the presence of the marker of claim 1, comprising the steps of: (a) contacting a biological sample containing albumin with a predetermined excess quantity of a salt of a metal selected from the group consisting of V, As, Co, Sb, Cr, Mo, Mn, Ba, Zn, Ni, Hg, Cd, Fe, Pb, Au and Ag, to form a mixture containing bound metal ions and unbound metal ions, (b) contacting said mixture with an aqueous color forming compound solution to form a colored solution, wherein said compound is capable of forming color when bound to said metal ion, (c) determining the color intensity of said colored solution to detect the presence of unbound metal ions to provide a measure of bound metal ions, and (d) correlating the amount of bound metal ions to a known value to determine the quantity of the marker present.

18. The method of claim 17, further comprising diluting said colored solution with an aqueous solution isosmotic with blood serum or plasma prior to step (c).

19. The method of claim 17, wherein said color forming compound is ferrozine.

20. The method of claim 17, wherein said aqueous color forming compound comprises the compound Asp-Ala-His-Lys-R, wherein R is any group capable of forming color when bound to said metal ion.

21. The method of claim 17, wherein said steps (b) and (c) are conducted in a pH range of 7to 9.

22. The method of claim 17, wherein said steps (b) and (c) are conducted using a spectrophotometer.

23. The method of claim 17, wherein said sample is serum or plasma.

24. The method of claim 17, wherein said sample is purified albumin.

25. The method of claim 17, wherein said metal ion salt is a salt of cobalt.

26. The method of claim 12, wherein said immunological assay is conducted using an antibody specific to an antigen comprising the compound Asp-Ala-His-Lys-R, wherein R is said metal ion.

27. The method of claim 26, wherein said antibody possesses known fluorescent properties.

28. The method of claim 12, wherein said immunological assay is conducted using an antibody to human serum albumin.

29. A method for detecting and quantifying the presence of the marker of claim 1, comprising the steps of: (a) detecting the amount of copper ions present in a purified albumin sample, and (b) correlating the quantity of copper ions present with a known value to determine the quantity of the marker present.

30. The method of claim 29, wherein said detecting step is conducted using atomic absorption or atomic emission spectroscopy.

31. The method of claim 29, wherein said detecting step is conducted using an immunological assay.

32 The method of claim 31, wherein said immunological assay is conducted using an antibody specific to an antigen comprising the compound Asp-Ala-His-Lys-R, wherein R is copper.

33. A method for detecting and quantifying the presence of the marker of claim 1, comprising the steps of: (a) contacting a purified albumin sample with an aqueous color forming compound solution to form a colored solution, wherein said compound is capable of forming color when bound to copper, (b) determining the color intensity of said colored solution to determine the amount copper in said sample, and (c) correlating the amount of copper to a known value to determine the quantity of the marker present.

34. The method of claim 33, further comprising diluting said colored solution with an aqueous solution isosmotic with blood serum or plasma prior to step (b).

35. The method of claim 33, wherein said color forming compound is ferrozine.

36. The method of claim 33, wherein said steps (a) and (b) are conducted in a pH range of 7to 9.

37. The method of claim 33, wherein said step (b) is conducted using a spectrophotometer.

38. The method of claim 31, wherein said immunological assay is conducted using an antibody to modified albumin, said albumin having been modified by mixture with copper ions.

39. The method of claim 38, wherein said antibody possesses known fluorescent properties.

40. A compound selected from the group consisting of Asp-Ala-His-Lys-R, wherein R is any chemical group capable of being detected when bound to any compound capable of binding to the N-terminus of naturally occurring human albumin.

41. An antibody to the marker of claim 1.

42. An immunological assay conducted using as an antigen the marker of claim 1.

43. An immunological assay conducted using an antibody to the marker of claim 1.

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L9: Entry 4 of 21 File: PGPB Sep 9, 2004

PGPUB-DOCUMENT-NUMBER: 20040175754
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20040175754 A1

TITLE: Diagnosis and monitoring of inflammation, ischemia and appendicitis

PUBLICATION-DATE: September 9, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Bar-Or, David	Englewood	CO	US	
Bar-Or, Raphael	Denver	CO	US	
Winkler, James V.	Denver	CO	US	
Yukl, Richard L.	Denver	CO	US	

US-CL-CURRENT: 435/7.1

CLAIMS:

We claim:

1. A method of diagnosing or monitoring inflammation in an animal comprising: (a) determining the quantity of a post-translationally modified protein, other than phosphorylated tau, present in a body fluid of the animal; and (b) determining if the quantity of the post-translationally modified protein is significantly altered compared to its level in the same body fluid from normal animals to determine if inflammation is present.

2. The method of claim 1 wherein the body fluid is serum or plasma.

4. The method of claim 1 wherein the protein is phosphorylated.

5. The method of claim 1 wherein the protein is cysteinylated.

6. The method of claim 1 wherein the quantities of two or more post-translationally modified proteins in one or more body fluids are determined.

7. The method of claim 1 wherein the method is used to diagnose or monitor the inflammation associated with sepsis.

8. The method of claim 1 wherein the method is used to diagnose or monitor the inflammation associated with a respiratory disease.

9. The method of claim 8 wherein the method is used to diagnose or monitor the inflammation associated with adult respiratory distress syndrome or chronic obstructive pulmonary disease.

10. A method of diagnosing or monitoring general inflammation in an animal comprising: (a) determining the quantity of a post-translationally modified protein which is a protein marker of general inflammation, other than phosphorylated tau, present in a body fluid of the animal; and (b) determining if the quantity of the post-translationally modified protein is significantly altered compared to its level in the same body fluid from normal animals to determine if inflammation is present.

11. The method of claim 10 wherein the quantities of two or more post-translationally modified proteins in one or more body fluids are determined.

12. The method of claim 10 wherein the body fluid is serum or plasma.

13. The method of claim 10 wherein the protein is phosphorylated.

14. The method of claim 10 wherein the protein is cysteinylated.

15. The method of claim 10 wherein the protein is albumin.

16. The method of claim 15 wherein the albumin is phosphorylated.

17. The method of claim 15 wherein the albumin is cysteinylated.

18. The method of claim 10 further comprising: (c) determining the quantity of a post-translationally modified indicator protein, other than phosphorylated tau, present in a body fluid of the animal; and (d) determining if the quantity of the post-translationally modified indicator protein is significantly altered compared to its level in the same body fluid from normal animals to determine if inflammation is present in an organ or tissue of the animal or is associated with a disease.

19. The method of claim 18 wherein the body fluid is serum or plasma.

20. The method of claim 18 wherein the indicator protein is phosphorylated.

21. The method of claim 18 wherein the indicator protein is cysteinylated.

22. The method of claim 18 wherein the quantities of two or more post-translationally modified indicator proteins in one or more body fluids are determined.

23. A method of diagnosing or monitoring inflammation in an animal comprising: (a) determining the quantity of a post-translationally modified indicator protein, other than phosphorylated tau, present in a body fluid of the animal; and (b) determining if the quantity of the post-translationally modified indicator protein is significantly altered compared to its level in the same body fluid from normal animals to determine if inflammation is present.

24. The method of claim 23 wherein the body fluid is serum or plasma.

25. The method of claim 23 wherein the indicator protein is phosphorylated.

26. The method of claim 23 wherein the indicator protein is cysteinylated.

27. The method of claim 23 wherein the quantities of two or more post-

translationally modified indicator proteins in one or more body fluids are determined.

28. A method of diagnosing or monitoring inflammation in an animal comprising: (a) determining the quantity of a post-translationally modified organ-specific or tissue-specific protein, other than phosphorylated tau, present in a body fluid of the animal; and (b) determining if the quantity of the post-translationally modified organ-specific or tissue-specific protein is significantly altered compared to its level in the same body fluid from normal animals to determine if inflammation is present in an organ or tissue.

29. The method of claim 28 wherein the body fluid is serum or plasma.

30. The method of claim 28 wherein the protein is phosphorylated.

31. The method of claim 28 wherein the protein is cysteinylated.

32. The method of claim 28 wherein the quantities of two or more post-translationally modified organ-specific or tissue-specific proteins in one or more body fluids are determined.

33. A method of diagnosing or monitoring inflammation in an animal comprising: (a) determining the quantity of a post-translationally modified disease-specific protein, other than phosphorylated tau, present in a body fluid of the animal; and (b) determining if the quantity of the post-translationally modified protein is significantly altered compared to its level in the same body fluid from normal animals to determine if inflammation associated with a disease is present.

34. The method of claim 33 wherein the body fluid is serum or plasma.

35. The method of claim 33 wherein the protein is phosphorylated.

36. The method of claim 33 wherein the protein is cysteinylated.

37. The method of claim 33 wherein the quantities of two or more post-translationally modified disease-specific proteins in one or more body fluids are determined.

38. The method of any one of claims 1-37 wherein the quantity(ies) of the post-translationally modified protein(s) is(are) determined by a binding-partner assay.

39. The method of claim 38 wherein the binding-partner assay is an immunoassay.

40. A method of diagnosing or monitoring a disease comprising: determining the quantity(ies) of one or more post-translationally modified proteins by a method of any one of claims 1-37; obtaining one or more additional diagnostic parameters; and using the quantity(ies) of the one or more post-translationally modified protein(s) and the additional diagnostic parameter(s) to diagnose or monitor the disease.

41. The method of claim 40 wherein the quantity(ies) of the post-translationally modified protein(s) is(are) determined by a binding-partner assay.

42. The method of claim 41 wherein the binding-partner assay is an immunoassay.

43. The method of claim 41 wherein the binding-partner is an antibody or an aptamer.

44. A method of diagnosing or monitoring ischemia in an organ or tissue of an animal comprising: (a) determining the quantity of a post-translationally modified organ-specific or tissue-specific protein, other than phosphorylated tau, present in a body fluid of the animal without denaturing the protein prior to making the determination; and (b) determining if the quantity of the post-translationally modified protein is significantly altered compared to its level in the same body fluid from normal animals to determine if ischemia is present in the organ or tissue.

45. The method of claim 44 wherein the body fluid is serum or plasma.

46. The method of claim 44 wherein the protein is phosphorylated.

47. The method of claim 44 wherein the protein is cysteinylated.

48. The method of claim 44 wherein the quantities of two or more post-translationally modified organ-specific or tissue-specific proteins in one or more body fluids are determined.

49. The method of claim 44 further comprising determining the quantity of a post-translationally modified protein which is a general marker of ischemia present in a body fluid from the animal.

50. The method of claim 49 wherein the body fluid is serum or plasma.

51. The method of claim 49 wherein the protein is phosphorylated.

52. The method of claim 49 wherein the protein is cysteinylated.

53. The method of claim 49 wherein the protein is albumin.

54. The method of claim 53 wherein the albumin is phosphorylated.

55. The method of claim 53 wherein the albumin is cysteinylated.

56. The method of claim 49 wherein the quantities of two or more post-translationally modified proteins which are general markers of ischemia are determined to determine if ischemia is present.

57. The method of any one of claims 44-56 wherein the quantity(ies) of the post-translationally modified protein(s) is(are) determined by a binding-partner assay.

58. The method of claim 57 wherein the binding-partner assay is an immunoassay.

59. The method of any one of claims 44-56 further comprising; obtaining one or more additional diagnostic parameters of ischemia; and using the quantity(ies) of the one or more post-translationally modified proteins and the additional diagnostic parameter(s) to diagnose or monitor the ischemia.

60. The method of claim 59 wherein the quantity(ies) of the post-translationally modified protein(s) is(are) determined by a binding-partner assay.

61. The method of claim 60 wherein the binding-partner assay is an immunoassay.

62. A method of diagnosing or monitoring cardiac ischemia in an animal comprising:

(a) determining the quantity of a post-translationally modified heart-specific protein present in a body fluid of the animal without denaturing the protein prior to making the determination; and (b) determining if the quantity of the post-translationally modified heart-specific protein is significantly altered compared to its level in the same body fluid from normal animals to determine if ischemia is present.

63. The method of claim 62 wherein the body fluid is serum or plasma.

64. The method of claim 62 wherein the protein is phosphorylated.

65. The method of claim 62 wherein the protein is cysteinylated.

66. The method of claim 62 wherein the protein is post-translationally modified cardiac troponin I.

67. The method of claim 66 wherein the protein is phosphorylated cardiac troponin I.

68. The method of claim 66 wherein the protein is cysteinylated cardiac troponin I.

69. The method of claim 62 wherein the protein is post-translationally modified cardiac troponin T.

70. The method of claim 69 wherein the protein is phosphorylated troponin T.

71. The method of claim 69 wherein the protein is cysteinylated cardiac troponin T.

72. The method of claim 62 wherein the quantities of two or more post-translationally modified heart-specific proteins in one or more body fluids are determined.

73. The method of claim 62 wherein the quantity of a post-translationally modified protein which is a general marker of ischemia present in a body fluid is also determined.

74. The method of claim 73 wherein the body fluid is serum or plasma.

75. The method of claim 73 wherein the protein is phosphorylated.

76. The method of claim 73 wherein the protein is cysteinylated.

77. The method of claim 73 wherein the protein is albumin.

78. The method of claim 75 wherein the albumin is phosphorylated.

79. The method of claim 75 wherein the albumin is cysteinylated.

80. The method of claim 73 wherein the quantities of two or more post-translationally modified proteins which are general markers of ischemia are determined.

81. The method of any one of claims 62-80 wherein the quantity(ies) of the post-translationally modified protein(s) is(are) determined by a binding-partner assay.

82. The method of claim 81 wherein the binding-partner assay is an immunoassay.

83. The method of any one of claims 62-80 further comprising; obtaining one or more additional diagnostic parameters of cardiac ischemia; and using the quantity(ies) of the one or more post-translationally modified proteins and the additional diagnostic parameter(s) to diagnose or monitor the ischemia.

84. The method of claim 83 wherein the additional diagnostic parameter is an electrocardiogram, a cardiac troponin I level, a cardiac troponin T level, or combinations of the foregoing.

85. The method of claims 83 wherein the quantity(ies) of the post-translationally modified protein(s) is(are) determined by a binding-partner assay.

86. The method of claim 85 wherein the binding-partner assay is an immunoassay.

87. A method for the early diagnosis of cardiac ischemia in an animal comprising performing the steps of the method of any one of claims 62-80 within the first 24 hours after the onset of symptoms indicative of cardiac ischemia.

88. The method of claim 87 wherein the steps of the method of any one of claims 62-80 are performed within the first 12 hours after the onset of symptoms indicative of cardiac ischemia.

89. The method of claim 87 wherein the quantity(ies) of the post-translationally modified protein(s) is(are) determined by a binding-partner assay.

90. The method of claim 89 wherein the binding-partner assay is an immunoassay.

91. The method of claim 87 further comprising; obtaining one or more additional diagnostic parameters of cardiac ischemia; and using the quantity(ies) of the one or more post-translationally modified proteins and the additional diagnostic parameter(s) to diagnose or monitor the ischemia.

92. The method of claim 91 wherein the additional diagnostic parameter is an electrocardiogram, a cardiac troponin I level, a cardiac troponin T level, or combinations of the foregoing.

93. The method of claim 88 wherein the quantity(ies) of the post-translationally modified protein(s) is(are) determined by a binding-partner assay.

94. The method of claim 93 wherein the binding-partner assay is an immunoassay.

95. The method of claim 88 further comprising; obtaining one or more additional diagnostic parameters of cardiac ischemia; and using the quantity(ies) of the one or more post-translationally modified proteins and the additional diagnostic parameter(s) to diagnose or monitor the ischemia.

96. The method of claim 95 wherein the additional diagnostic parameter is an electrocardiogram, a cardiac troponin I level, a cardiac troponin T level, or combinations of the foregoing.

97. A method of diagnosing or monitoring placental ischemia in a pregnant animal comprising: (a) determining the quantity of a post-translationally modified pregnancy-associated protein present in a body fluid of the animal; and (b) determining if the quantity of the post-translationally modified protein is

significantly altered compared to its level in the same body fluid from normal pregnant animals to determine if ischemia is present.

98. The method of claim 97 wherein the body fluid is maternal serum or plasma.

99. The method of claim 97 wherein the protein is phosphorylated.

100. The method of claim 97 wherein the protein is cysteinylated.

101. The method of claim 97 wherein the protein is post-translationally modified .beta.-human chorionic gonadotropin, .alpha.-fetoprotein, pregnancy-associated protein 1A, erythropoietin, angiotensin, or combinations of the foregoing

102. The method of claim 97 wherein the quantities of two or more post-translationally modified pregnancy-associated proteins in one or more body fluids are determined.

103. The method of claim 97 further comprising determining the quantity of a post-translationally modified protein which is a general marker of ischemia present in a body fluid.

104. The method of claim 103 wherein the body fluid is maternal serum or plasma.

105. The method of claim 103 wherein the protein is phosphorylated.

106. The method of claim 103 wherein the protein is cysteinylated.

107. The method of claim 103 wherein the protein is albumin.

108. The method of claim 107 wherein the protein is phosphorylated.

109. The method of claim 107 wherein the protein is cysteinylated.

110. The method of claim 103 wherein the quantities of two or more post-translationally modified proteins which are general markers of ischemia are determined.

111. The method of any one of claims 97-110 wherein the quantity(ies) of the post-translationally modified protein(s) is(are) determined by a binding-partner assay.

112. The method of claim 111 wherein the binding-partner assay is an immunoassay.

113. The method of any one of claims 97-110 further comprising; obtaining one or more additional diagnostic parameters of placental ischemia; and using the quantity (ies) of the one or more post-translationally modified proteins and the additional diagnostic parameter(s) to diagnose or monitor the placental ischemia.

114. The method of claim 113 wherein the quantity(ies) of the post-translationally modified protein(s) is(are) determined by a binding-partner assay.

115. The method of claim 114 wherein the binding-partner assay is an immunoassay.

116. A method of diagnosing or monitoring ischemia in an animal comprising: (a) determining the quantity present in a body fluid of a phosphorylated protein

constituent of the body fluid; and (b) determining if the quantity of the phosphorylated protein is significantly altered compared to its level in the same body fluid from normal animals to determine if ischemia is present.

117. The method of claim 116 wherein the body fluid is serum or plasma.

118. The method of claim 116 wherein the phosphorylated protein is phosphorylated albumin.

119. The method of claim 116 wherein the ischemia is cardiac ischemia.

120. The method of claim 116 wherein the quantity of the phosphorylated protein is determined by a binding-partner assay.

121. The method of claim 120 wherein the binding-partner assay is an immunoassay.

122. The method of any one of claims 116-121 further comprising; obtaining one or more additional diagnostic parameters of ischemia; and using the quantity of phosphorylated protein and the additional diagnostic parameter(s) to diagnose or monitor the ischemia.

123. The method of claim 122 wherein the ischemia is cardiac ischemia and the additional diagnostic parameter is an electrocardiogram, a cardiac troponin I level, a cardiac troponin T level, or combinations of the foregoing.

124. A method of diagnosing or monitoring ischemia in an animal comprising: (a) determining the quantity present in a body fluid of a phosphorylated protein, wherein the phosphorylation of the protein occurred at least in part by substrate phosphorylation; and (b) determining if the quantity of the phosphorylated protein is significantly altered compared to its level in the same body fluid from normal animals to determine if ischemia is present.

125. The method of claim 124 wherein the body fluid is serum or plasma.

126. The method of claim 124 wherein the phosphorylated protein is phosphorylated albumin.

127. The method of claim 124 wherein the ischemia is cardiac ischemia.

128. The method of claim 127 wherein the phosphorylated protein is troponin I.

129. The method of claim 127 wherein the phosphorylated protein is troponin T.

130. The method of claim 124 wherein the quantity of the phosphorylated protein is determined by a binding-partner assay.

131. The method of claim 130 wherein the binding-partner assay is an immunoassay.

132. The method of any one of claims 124-131 further comprising; obtaining one or more additional diagnostic parameters of ischemia; and using the quantity of phosphorylated protein and the additional diagnostic parameter(s) to diagnose or monitor the ischemia.

133. The method of claim 132 wherein the ischemia is cardiac ischemia and the additional diagnostic parameter is an electrocardiogram, a cardiac troponin I

level, a cardiac troponin T level, or combinations of the foregoing.

134. A method of diagnosing or monitoring ischemia in an animal comprising: (a) determining the quantity of a cysteinylated protein present in a body fluid of the animal; and (b) determining if the quantity of the cysteinylated protein is significantly altered compared to its level in the same body fluid from normal animals to determine if ischemia is present.

135. The method of claim 134 wherein the body fluid is serum or plasma.

136. The method of claim 134 wherein the cysteinylated protein is cysteinylated albumin.

137. The method of claim 134 wherein the ischemia is cardiac ischemia.

138. The method of claim 134 wherein the ischemia is bowel ischemia.

139. The method of any one of claims 134-138 wherein the quantity of the cysteinylated protein is determined by a binding-partner assay.

140. The method of claim 139 wherein the binding-partner assay is an immunoassay.

141. The method of any one of claims 134-138 further comprising; obtaining one or more additional diagnostic parameters of ischemia; and using the quantity of the cysteinylated protein and the additional diagnostic parameter(s) to diagnose or monitor the ischemia.

142. The method of claim 141 wherein the quantity of the cysteinylated protein is determined by a binding-partner assay.

143. The method of claim 142 wherein the binding-partner assay is an immunoassay.

144. The method of claim 143 wherein the ischemia is cardiac ischemia and the additional diagnostic parameter is an electrocardiogram, a cardiac troponin I level, a cardiac troponin T level, or combinations of the foregoing.

145. A method of diagnosing or monitoring placental ischemia in a pregnant animal comprising: (a) determining the quantity of a cysteinylated protein present in a body fluid of the animal; and (b) determining if the quantity of the cysteinylated protein is significantly altered compared to its level in the same body fluid from normal pregnant animals to determine if placental ischemia is present.

146. The method of claim 145 wherein the body fluid is maternal serum or plasma.

147. The method of claim 145 wherein the cysteinylated protein is cysteinylated albumin.

148. The method of any one of claims 145-147 wherein the quantity of the cysteinylated protein is determined by a binding-partner assay.

149. The method of claim 148 wherein the binding-partner assay is an immunoassay.

150. The method of any one of claims 145-147 further comprising; obtaining one or more additional diagnostic parameters of placental ischemia; and using the quantity of the cysteinylated protein and the additional diagnostic parameter(s) to diagnose

or monitor the placental ischemia.

151. The method of claim 150 wherein the quantity of the cysteinylated protein is determined by a binding-partner assay.

152. The method of claim 151 wherein the binding-partner assay is an immunoassay.

153. A method of diagnosing, monitoring or predicting multiple organ failure in an animal comprising: (a) determining the quantity of a post-translationally modified protein present in a body fluid of the animal; and (b) determining if the quantity of the post-translationally modified protein is significantly altered compared to its level in the same body fluid from normal animals to determine if multiple organ failure is present or will develop.

154. The method of claim 153 wherein the body fluid is serum or plasma.

155. The method of claim 153 wherein the post-translationally-modified protein is a post-translationally modified albumin.

156. The method of claim 153 wherein the post-translationally-modified protein is a cysteinylated protein.

157. The method of claim 156 wherein the cysteinylated protein is cysteinylated albumin.

158. The method of any one of claims 153-157 wherein the quantity of the post-translationally-modified protein is determined by a binding-partner assay.

159. The method of claim 158 wherein the binding-partner assay is an immunoassay.

160. The method of any one of claims 153-157 further comprising; obtaining one or more additional diagnostic parameters of multiple organ failure; and using the quantity of the post-translationally-modified protein and the additional diagnostic parameter(s) to diagnose, monitor or predict the multiple organ failure.

161. The method of claim 160 wherein the quantity of the post-translationally-modified protein is determined by a binding-partner assay.

162. The method of claim 161 wherein the binding-partner assay is an immunoassay.

163. A binding partner specific for phosphorylated albumin.

164. A binding partner specific for a cysteinylated blood protein.

165. The binding partner of claim 164 which is specific for cysteinylated albumin.

166. A binding partner specific for a cysteinylated organ-specific or tissue-specific protein.

167. The binding partner of claim 166 which is specific for a cysteinylated heart-specific protein.

168. The binding partner of claim 167 which is specific for cysteinylated troponin I.

169. The binding partner of claim 167 which is specific for cysteinylated troponin T.

170. A binding partner specific for a post-translationally modified pregnancy-associated protein.

171. The binding partner of claim 170 which is specific for a cysteinylated pregnancy-associated protein.

172. The binding partner of claim 171 which is specific for cysteinylated .beta.-human chorionic gonadotropin, cysteinylated .alpha.-fetoprotein, cysteinylated pregnancy-associated protein 1A, cysteinylated erythropoietin or cysteinylated angiotensin.

173. The binding partner of claim 170 which is specific for a phosphorylated pregnancy-associated protein.

174. The binding partner of claim 173 which is specific for phosphorylated .beta.-human chorionic gonadotropin, phosphorylated .alpha.-fetoprotein, phosphorylated pregnancy-associated protein 1A, phosphorylated erythropoietin or phosphorylated angiotensin.

175. The binding partner of claim 165-174 which is an antibody.

176. The binding partner of claim 165-174 which is an aptamer.

177. A kit comprising: a container holding a binding partner specific for a post-translationally modified protein other than phosphorylated tau; and instructions directing that the binding partner is to be used to determine the quantity of the post-translationally modified protein present in a body fluid of an animal in order to diagnose or monitor inflammation.

178. The kit of claim 177 wherein the protein is a post-translationally protein which can be used to diagnose or monitor general inflammation.

179. The kit of claim 178 wherein the post-translationally-modified protein is a post-translationally modified albumin.

180. The kit of claim 179 wherein the post-translationally-modified albumin is phosphorylated albumin.

181. The kit of claim 179 wherein the post-translationally-modified albumin is cysteinylated albumin.

182. The kit of claim 177 wherein the post-translationally modified protein is a post-translationally-modified indicator protein.

183. The kit of claim 182 wherein the post-translationally modified indicator protein is a post-translationally-modified organ-specific or tissue-specific protein.

184. The kit of claim 182 wherein the post-translationally modified indicator protein is a post-translationally-modified disease-specific protein.

185. The kit of claim 177 wherein the post-translationally-modified protein is a phosphorylated protein

186. The kit of claim 177 wherein the post-translationally-modified protein is a cysteinylated protein.

187. The kit of any one of claims 177-186 further comprising one or more additional containers holding one or more additional binding partners specific for one or more additional post-translationally modified proteins, other than phosphorylated tau, and the instructions direct that the additional binding partner(s) is(are) to be used to determine the quantity(ies) of the one or more additional post-translationally modified protein(s) present in one or more body fluids of an animal in order to diagnose or monitor inflammation.

188. The kit of any one of claims 177-186 wherein the binding partner(s) is(are) antibodies.

189. The kit of claim 187 wherein the binding partners are antibodies.

190. The kit of any one of claims 177-186 wherein the binding partner(s) is(are) aptamers.

191. The kit of claim 187 wherein the binding partners are aptamers.

192. A kit comprising: a container holding a binding partner specific for a post-translationally modified organ-specific or tissue-specific protein, other than phosphorylated tau; and instructions directing that the binding partner is to be used to determine the quantity of the post-translationally modified protein present in a body fluid of an animal in such a manner that the protein is not denatured prior to the determination in order to diagnose or monitor ischemia of the organ or tissue.

193. The kit of claim 192 wherein the post-translationally-modified protein is a phosphorylated protein.

194. The kit of claim 192 wherein the post-translationally-modified protein is a cysteinylated protein.

195. The kit of claim 192 wherein the post-translationally-modified protein is a post-translationally modified heart-specific protein.

196. The kit of claim 195 wherein the post-translationally-modified heart-specific protein is a post-translationally modified troponin I.

197. The kit of claim 196 wherein the post-translationally-modified troponin I is phosphorylated troponin I.

198. The kit of claim 196 wherein the post-translationally-modified troponin I is cysteinylated troponin I.

199. The kit of claim 195 wherein the post-translationally-modified heart-specific protein is a post-translationally modified troponin T.

200. The kit of claim 199 wherein the post-translationally-modified troponin T is phosphorylated troponin T.

201. The kit of claim 199 wherein the post-translationally-modified troponin T is cysteinylated troponin T.

202. The kit of any one of claims 192-201 further comprising one or more additional containers holding one or more additional binding partners specific for one or more additional post-translationally modified proteins, and the instructions direct that the additional binding partner(s) is(are) to be used to determine the quantity(ies) of the one or more additional post-translationally modified protein(s) present in a body fluid of an animal in such a manner that the protein is not denatured prior to the determination in order to diagnose or monitor ischemia of the organ or tissue.

203. The kit of any one of claims 192-201 wherein the binding partner(s) is(are) antibodies.

204. The kit of claim 202 wherein the binding partners are antibodies.

205. The kit of any one of claims 192-201 wherein the binding partner(s) is(are) aptamers.

206. The kit of claim 202 wherein the binding partners are aptamers.

207. A kit comprising: a container holding a binding partner specific for a post-translationally modified pregnancy-associated protein; and instructions directing that the binding partner is to be used to determine the quantity of the post-translationally modified protein present in a body fluid of a pregnant animal in order to diagnose or monitor placental ischemia.

208. The kit of claim 207 wherein the post-translationally modified pregnancy-associated protein is a cysteinylated protein.

209. The kit of claim 207 wherein the post-translationally modified pregnancy-associated protein is a phosphorylated protein.

210. The kit of claim 207 wherein the post-translationally modified pregnancy-associated protein is a post-translationally modified .beta.-human chorionic gonadotropin, .alpha.-fetoprotein, pregnancy-associated protein 1A, erythropoietin, angiotensin, or combinations of the foregoing.

211. The kit of claim 210 wherein the post-translationally modified pregnancy-associated protein is a cysteinylated modified i-human chorionic gonadotropin, .alpha.-fetoprotein, pregnancy-associated protein 1A, erythropoietin, angiotensin, or combinations of the foregoing.

212. The kit of claim 210 wherein the post-translationally modified pregnancy-associated protein is a phosphorylated modified i-human chorionic gonadotropin, .alpha.-fetoprotein, pregnancy-associated protein 1A, erythropoietin, angiotensin, or combinations of the foregoing.

213. The kit of claims 207 further comprising one or more additional containers holding one or more additional binding partners specific for one or more additional post-translationally modified proteins, and the instructions direct that the additional binding partner(s) is(are) to be used to determine the quantity(ies) of the one or more additional post-translationally modified protein(s) present in a body fluid of a pregnant animal in order to diagnose or monitor placental ischemia.

214. The kit of any one of claims 207-213 wherein the binding partner is an antibody.

215. The kit of any one of claims 205-213 wherein the binding partner is an aptamer.

216. A kit comprising: a container holding a binding partner specific for a phosphorylated protein constituent of a body fluid; and instructions directing that the binding partner is to be used to determine the quantity of the phosphorylated protein present in a body fluid of an animal in order to diagnose or monitor ischemia.

217. The kit of claim 216 wherein the phosphorylated protein is phosphorylated albumin.

218. The kit of claims 216 further comprising one or more additional containers holding one or more additional binding partners specific for one or more additional post-translationally modified proteins, and the instructions direct that the additional binding partner(s) is(are) to be used to determine the quantity(ies) of the one or more additional post-translationally modified protein(s) present in a body fluid of an animal in order to diagnose or monitor ischemia.

219. The kit of claim 216, 217 or 218 wherein the binding partner is an antibody.

220. The kit of claim 216, 217 or 218 wherein the binding partner is an aptamer.

221. A kit comprising: a container holding a binding partner specific for a cysteinylated protein; and instructions directing that the binding partner is to be used to determine the quantity of the cysteinylated protein present in a body fluid of an animal in order to diagnose or monitor ischemia.

222. The kit of claim 221 wherein the cysteinylated protein is cysteinylated albumin.

223. The kit of claims 221 further comprising one or more additional containers holding one or more additional binding partners specific for one or more additional post-translationally modified proteins, and the instructions direct that the additional binding partner(s) is(are) to be used to determine the quantity(ies) of the one or more additional post-translationally modified protein(s) present in a body fluid of an animal in order to diagnose or monitor ischemia.

224. The kit of claim 221, 222 or 223 wherein the binding partner is an antibody.

225. The kit of claim 221, 222 or 223 wherein the binding partner is an aptamer.

226. A kit comprising: a container holding a binding partner specific for a cysteinylated protein; and instructions directing that the binding partner is to be used to determine the quantity of the cysteinylated protein present in a body fluid of a pregnant animal in order to diagnose or monitor placental ischemia.

227. The kit of claim 226 wherein the cysteinylated protein is cysteinylated albumin.

228. The kit of claims 226 further comprising one or more additional containers holding one or more additional binding partners specific for one or more additional post-translationally modified proteins, and the instructions direct that the additional binding partner(s) is(are) to be used to determine the quantity(ies) of the one or more additional post-translationally modified protein(s) present in a body fluid of a pregnant animal in order to diagnose or monitor placental ischemia.

229. The kit of claim 226, 227 or 228 wherein the binding partner is an antibody.

230. The kit of claim 226, 227 or 228 wherein the binding partner is an aptamer.

231. A kit comprising: a container holding a binding partner specific for a post-translationally modified protein; and instructions directing that the binding partner is to be used to determine the quantity of the post-translationally modified protein present in a body fluid of an animal in order to diagnose, monitor or predict multiple organ failure.

232. The kit of claim 231 wherein the post-translationally modified protein is a cysteinylated protein.

233. The kit of claim 232 wherein the cysteinylated protein is cysteinylated albumin.

234. The kit of claim 231 further comprising one or more additional containers holding one or more additional binding partners specific for one or more additional post-translationally modified proteins, and the instructions direct that the additional binding partner(s) is(are) to be used to determine the quantity(ies) of the one or more additional post-translationally modified protein(s) present in a body fluid of an animal in order to diagnose, monitor or predict multiple organ failure.

235. The kit of any one of claims 231-234 wherein the binding partner is an antibody.

236. The kit of any one of claims 231-234 wherein the binding partner is an aptamer.

237. A kit comprising: a container holding a binding partner specific for a phosphorylated protein other than phosphorylated tau; and a container holding a phosphatase inhibitor or a mixture of phosphatase inhibitors.

238. The kit of claim 237 further comprising one or more additional containers holding one or more additional binding partners specific for one or more additional post-translationally modified proteins.

239. The kit of claim 237 or 238 wherein the binding partner is an antibody.

240. The kit of claim 237 or 238 wherein the binding partner is an aptamer.

241. A method of diagnosing appendicitis in an animal comprising the following steps: (a) obtaining a first body fluid from the animal and obtaining a second body fluid from the animal, wherein the first and second body fluids may be the same or different; (b) determining if the quantity of orthohydroxyhippuric acid (OHHA) present in the first body fluid of the animal is significantly elevated compared to its level in the same body fluid from normal animals; (c) determining if the quantity of a marker of general inflammation present in the second body fluid of the animal is significantly altered compared to its level in the same body fluid from normal animals; and (d) correlating the results obtained in steps (b) and (c) to the presence or absence of appendicitis.

242. The method of claim 241 wherein the first body fluid is urine.

243. The method of claim 242 wherein step (b) comprises: mixing a portion of the urine from the animal being diagnosed with a color-producing reagent that produces a color when it is contacted with OHHA; incubating the urine and the color-producing reagent for a time sufficient to allow production of the color; and

comparing the color produced to a color comparison chart or to the colors produced by standards comprising known amounts of OHHA to determine if the quantity of OHHA present in the urine is significantly elevated.

244. The method of claim 243 wherein the color-producing reagent is ferric ions bonded to silica.

245. The method of claim 241 wherein step (b) is performed using a binding partner assay.

246. The method of claim 241 wherein step (c) is performed using a binding partner assay.

247. The method of claim 241 wherein the second body fluid is urine.

248. The method of claim 247 wherein the marker of general inflammation is interleukin 8.

249. The method of claim 241 wherein the second body fluid is serum or plasma.

250. The method of claim 249 wherein the marker of general inflammation is leukocyte count.

251. The method of claim 249 wherein the marker of general inflammation is neutrophil band count.

252. The method of claim 241 wherein the marker of general inflammation is a post-translationally modified protein.

253. The method of claim 249 wherein the marker of general inflammation is a post-translationally modified protein

254. The method of claim 253 wherein the post-translationally modified protein is phosphorylated albumin.

255. The method of claim 253 wherein the post-translationally modified protein is cysteinylated albumin.

256. The method of any one of claims 241-255 wherein the animal is a human.

257. A kit for diagnosing appendicitis comprising Parts (A) and (B), wherein: Part (A) comprises at least one container holding a reagent useful for determining if the quantity of orthohydroxyhippuric acid (OHHA) present in a body fluid of an animal is significantly elevated compared to its level in the same body fluid from normal animals; and Part (B) comprises at least one container holding a reagent useful for determining if the quantity of a marker of general inflammation present in a body fluid of the animal is significantly altered compared to its level in the same body fluid from normal animals.

258. The kit of claim 257 wherein Part (A) comprises a container holding a color-producing reagent that produces a color when contacted with OHHA.

259. The kit of claim 258 wherein the color-producing reagent is ferric ions bonded to silica.

260. The kit of claim 258 or 259 further comprising a color comparison chart.

261. The kit of claim 258 or 259 further comprising one or more containers holding standards comprising known amounts of OHHA.

262. The kit of claim 257 wherein Part (A) comprises a container holding a binding partner specific for OHHA.

263. The kit of claim 257 wherein Part (B) comprises a container holding a binding partner specific for a post-translationally modified protein.

264. The kit of claim 263 wherein the post-translationally modified protein is phosphorylated albumin.

265. The kit of claim 263 wherein the post-translationally modified protein is cysteinylated albumin.

266. The kit of claim 257 wherein Part (B) comprises a container holding a binding partner specific for a cytokine.

267. The kit of claim 266 wherein the cytokine is interleukin 8.

268. A kit for diagnosing appendicitis comprising: at least one container holding a reagent useful for determining if the quantity of marker of general inflammation present in a body fluid of an animal is significantly altered compared to its level in the same body fluid from normal animals; and instructions directing how the reagent is to be used to diagnose appendicitis.

269. The kit of claim 268 wherein the reagent is a binding partner specific for a marker of general inflammation.

270. The kit of claim 269 comprising a container holding a binding partner specific for a post-translationally modified protein.

271. The kit of claim 270 wherein the post-translationally modified protein is phosphorylated albumin.

272. The kit of claim 270 wherein the post-translationally modified protein is cysteinylated albumin.

273. The kit of claim 269 comprising a container holding a binding partner specific for a cytokine.

274. The kit of claim 273 wherein the cytokine is interleukin 8.

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CLAIMS:

We claim:

1. A method of diagnosing or monitoring inflammation in an animal comprising: (a) determining the quantity of a post-translationally modified protein, other than phosphorylated tau, present in a body fluid of the animal; and (b) determining if the quantity of the post-translationally modified protein is significantly altered compared to its level in the same body fluid from normal animals to determine if inflammation is present.

2. The method of claim 1 wherein the body fluid is serum or plasma.

4. The method of claim 1 wherein the protein is phosphorylated.

5. The method of claim 1 wherein the protein is cysteinylated.

6. The method of claim 1 wherein the quantities of two or more post-translationally modified proteins in one or more body fluids are determined.

7. The method of claim 1 wherein the method is used to diagnose or monitor the inflammation associated with sepsis.

8. The method of claim 1 wherein the method is used to diagnose or monitor the inflammation associated with a respiratory disease.

9. The method of claim 8 wherein the method is used to diagnose or monitor the inflammation associated with adult respiratory distress syndrome or chronic obstructive pulmonary disease.

10. A method of diagnosing or monitoring general inflammation in an animal comprising: (a) determining the quantity of a post-translationally modified protein which is a protein marker of general inflammation, other than phosphorylated tau, present in a body fluid of the animal; and (b) determining if the quantity of the post-translationally modified protein is significantly altered compared to its level in the same body fluid from normal animals to determine if inflammation is present.

11. The method of claim 10 wherein the quantities of two or more post-translationally modified proteins in one or more body fluids are determined.

12. The method of claim 10 wherein the body fluid is serum or plasma.

13. The method of claim 10 wherein the protein is phosphorylated.

14. The method of claim 10 wherein the protein is cysteinylated.

15. The method of claim 10 wherein the protein is albumin.

16. The method of claim 15 wherein the albumin is phosphorylated.

17. The method of claim 15 wherein the albumin is cysteinylated.

18. The method of claim 10 further comprising: (c) determining the quantity of a post-translationally modified indicator protein, other than phosphorylated tau, present in a body fluid of the animal; and (d) determining if the quantity of the post-translationally modified indicator protein is significantly altered compared to its level in the same body fluid from normal animals to determine if inflammation is present in an organ or tissue of the animal or is associated with a disease.

19. The method of claim 18 wherein the body fluid is serum or plasma.

20. The method of claim 18 wherein the indicator protein is phosphorylated.

21. The method of claim 18 wherein the indicator protein is cysteinylated.

22. The method of claim 18 wherein the quantities of two or more post-translationally modified indicator proteins in one or more body fluids are determined.

23. A method of diagnosing or monitoring inflammation in an animal comprising: (a) determining the quantity of a post-translationally modified indicator protein, other than phosphorylated tau, present in a body fluid of the animal; and (b) determining if the quantity of the post-translationally modified indicator protein is significantly altered compared to its level in the same body fluid from normal animals to determine if inflammation is present.

24. The method of claim 23 wherein the body fluid is serum or plasma.

25. The method of claim 23 wherein the indicator protein is phosphorylated.

26. The method of claim 23 wherein the indicator protein is cysteinylated.

27. The method of claim 23 wherein the quantities of two or more post-

translationally modified indicator proteins in one or more body fluids are determined.

28. A method of diagnosing or monitoring inflammation in an animal comprising: (a) determining the quantity of a post-translationally modified organ-specific or tissue-specific protein, other than phosphorylated tau, present in a body fluid of the animal; and (b) determining if the quantity of the post-translationally modified organ-specific or tissue-specific protein is significantly altered compared to its level in the same body fluid from normal animals to determine if inflammation is present in an organ or tissue.

29. The method of claim 28 wherein the body fluid is serum or plasma.

30. The method of claim 28 wherein the protein is phosphorylated.

31. The method of claim 28 wherein the protein is cysteinylated.

32. The method of claim 28 wherein the quantities of two or more post-translationally modified organ-specific or tissue-specific proteins in one or more body fluids are determined.

33. A method of diagnosing or monitoring inflammation in an animal comprising: (a) determining the quantity of a post-translationally modified disease-specific protein, other than phosphorylated tau, present in a body fluid of the animal; and (b) determining if the quantity of the post-translationally modified protein is significantly altered compared to its level in the same body fluid from normal animals to determine if inflammation associated with a disease is present.

34. The method of claim 33 wherein the body fluid is serum or plasma.

35. The method of claim 33 wherein the protein is phosphorylated.

36. The method of claim 33 wherein the protein is cysteinylated.

37. The method of claim 33 wherein the quantities of two or more post-translationally modified disease-specific proteins in one or more body fluids are determined.

38. The method of any one of claims 1-37 wherein the quantity(ies) of the post-translationally modified protein(s) is(are) determined by a binding-partner assay.

39. The method of claim 38 wherein the binding-partner assay is an immunoassay.

40. A method of diagnosing or monitoring a disease comprising: determining the quantity(ies) of one or more post-translationally modified proteins by a method of any one of claims 1-37; obtaining one or more additional diagnostic parameters; and using the quantity(ies) of the one or more post-translationally modified protein(s) and the additional diagnostic parameter(s) to diagnose or monitor the disease.

41. The method of claim 40 wherein the quantity(ies) of the post-translationally modified protein(s) is(are) determined by a binding-partner assay.

42. The method of claim 41 wherein the binding-partner assay is an immunoassay.

43. The method of claim 41 wherein the binding-partner is an antibody or an aptamer.

44. A method of diagnosing or monitoring ischemia in an organ or tissue of an animal comprising: (a) determining the quantity of a post-translationally modified organ-specific or tissue-specific protein, other than phosphorylated tau, present in a body fluid of the animal without denaturing the protein prior to making the determination; and (b) determining if the quantity of the post-translationally modified protein is significantly altered compared to its level in the same body fluid from normal animals to determine if ischemia is present in the organ or tissue.

45. The method of claim 44 wherein the body fluid is serum or plasma.

46. The method of claim 44 wherein the protein is phosphorylated.

47. The method of claim 44 wherein the protein is cysteinylated.

48. The method of claim 44 wherein the quantities of two or more post-translationally modified organ-specific or tissue-specific proteins in one or more body fluids are determined.

49. The method of claim 44 further comprising determining the quantity of a post-translationally modified protein which is a general marker of ischemia present in a body fluid from the animal.

50. The method of claim 49 wherein the body fluid is serum or plasma.

51. The method of claim 49 wherein the protein is phosphorylated.

52. The method of claim 49 wherein the protein is cysteinylated.

53. The method of claim 49 wherein the protein is albumin.

54. The method of claim 53 wherein the albumin is phosphorylated.

55. The method of claim 53 wherein the albumin is cysteinylated.

56. The method of claim 49 wherein the quantities of two or more post-translationally modified proteins which are general markers of ischemia are determined to determine if ischemia is present.

57. The method of any one of claims 44-56 wherein the quantity(ies) of the post-translationally modified protein(s) is(are) determined by a binding-partner assay.

58. The method of claim 57 wherein the binding-partner assay is an immunoassay.

59. The method of any one of claims 44-56 further comprising; obtaining one or more additional diagnostic parameters of ischemia; and using the quantity(ies) of the one or more post-translationally modified proteins and the additional diagnostic parameter(s) to diagnose or monitor the ischemia.

60. The method of claim 59 wherein the quantity(ies) of the post-translationally modified protein(s) is(are) determined by a binding-partner assay.

61. The method of claim 60 wherein the binding-partner assay is an immunoassay.

62. A method of diagnosing or monitoring cardiac ischemia in an animal comprising:

(a) determining the quantity of a post-translationally modified heart-specific protein present in a body fluid of the animal without denaturing the protein prior to making the determination; and (b) determining if the quantity of the post-translationally modified heart-specific protein is significantly altered compared to its level in the same body fluid from normal animals to determine if ischemia is present.

63. The method of claim 62 wherein the body fluid is serum or plasma.

64. The method of claim 62 wherein the protein is phosphorylated.

65. The method of claim 62 wherein the protein is cysteinylated.

66. The method of claim 62 wherein the protein is post-translationally modified cardiac troponin I.

67. The method of claim 66 wherein the protein is phosphorylated cardiac troponin I.

68. The method of claim 66 wherein the protein is cysteinylated cardiac troponin I.

69. The method of claim 62 wherein the protein is post-translationally modified cardiac troponin T.

70. The method of claim 69 wherein the protein is phosphorylated troponin T.

71. The method of claim 69 wherein the protein is cysteinylated cardiac troponin T.

72. The method of claim 62 wherein the quantities of two or more post-translationally modified heart-specific proteins in one or more body fluids are determined.

73. The method of claim 62 wherein the quantity of a post-translationally modified protein which is a general marker of ischemia present in a body fluid is also determined.

74. The method of claim 73 wherein the body fluid is serum or plasma.

75. The method of claim 73 wherein the protein is phosphorylated.

76. The method of claim 73 wherein the protein is cysteinylated.

77. The method of claim 73 wherein the protein is albumin.

78. The method of claim 75 wherein the albumin is phosphorylated.

79. The method of claim 75 wherein the albumin is cysteinylated.

80. The method of claim 73 wherein the quantities of two or more post-translationally modified proteins which are general markers of ischemia are determined.

81. The method of any one of claims 62-80 wherein the quantity(ies) of the post-translationally modified protein(s) is(are) determined by a binding-partner assay.

82. The method of claim 81 wherein the binding-partner assay is an immunoassay.

83. The method of any one of claims 62-80 further comprising; obtaining one or more additional diagnostic parameters of cardiac ischemia; and using the quantity(ies) of the one or more post-translationally modified proteins and the additional diagnostic parameter(s) to diagnose or monitor the ischemia.

84. The method of claim 83 wherein the additional diagnostic parameter is an electrocardiogram, a cardiac troponin I level, a cardiac troponin T level, or combinations of the foregoing.

85. The method of claims 83 wherein the quantity(ies) of the post-translationally modified protein(s) is(are) determined by a binding-partner assay.

86. The method of claim 85 wherein the binding-partner assay is an immunoassay.

87. A method for the early diagnosis of cardiac ischemia in an animal comprising performing the steps of the method of any one of claims 62-80 within the first 24 hours after the onset of symptoms indicative of cardiac ischemia.

88. The method of claim 87 wherein the steps of the method of any one of claims 62-80 are performed within the first 12 hours after the onset of symptoms indicative of cardiac ischemia.

89. The method of claim 87 wherein the quantity(ies) of the post-translationally modified protein(s) is(are) determined by a binding-partner assay.

90. The method of claim 89 wherein the binding-partner assay is an immunoassay.

91. The method of claim 87 further comprising; obtaining one or more additional diagnostic parameters of cardiac ischemia; and using the quantity(ies) of the one or more post-translationally modified proteins and the additional diagnostic parameter(s) to diagnose or monitor the ischemia.

92. The method of claim 91 wherein the additional diagnostic parameter is an electrocardiogram, a cardiac troponin I level, a cardiac troponin T level, or combinations of the foregoing.

93. The method of claim 88 wherein the quantity(ies) of the post-translationally modified protein(s) is(are) determined by a binding-partner assay.

94. The method of claim 93 wherein the binding-partner assay is an immunoassay.

95. The method of claim 88 further comprising; obtaining one or more additional diagnostic parameters of cardiac ischemia; and using the quantity(ies) of the one or more post-translationally modified proteins and the additional diagnostic parameter(s) to diagnose or monitor the ischemia.

96. The method of claim 95 wherein the additional diagnostic parameter is an electrocardiogram, a cardiac troponin I level, a cardiac troponin T level, or combinations of the foregoing.

97. A method of diagnosing or monitoring placental ischemia in a pregnant animal comprising: (a) determining the quantity of a post-translationally modified pregnancy-associated protein present in a body fluid of the animal; and (b) determining if the quantity of the post-translationally modified protein is

significantly altered compared to its level in the same body fluid from normal pregnant animals to determine if ischemia is present.

98. The method of claim 97 wherein the body fluid is maternal serum or plasma.

99. The method of claim 97 wherein the protein is phosphorylated.

100. The method of claim 97 wherein the protein is cysteinylated.

101. The method of claim 97 wherein the protein is post-translationally modified .beta.-human chorionic gonadotropin, .alpha.-fetoprotein, pregnancy-associated protein 1A, erythropoietin, angiotensin, or combinations of the foregoing

102. The method of claim 97 wherein the quantities of two or more post-translationally modified pregnancy-associated proteins in one or more body fluids are determined.

103. The method of claim 97 further comprising determining the quantity of a post-translationally modified protein which is a general marker of ischemia present in a body fluid.

104. The method of claim 103 wherein the body fluid is maternal serum or plasma.

105. The method of claim 103 wherein the protein is phosphorylated.

106. The method of claim 103 wherein the protein is cysteinylated.

107. The method of claim 103 wherein the protein is albumin.

108. The method of claim 107 wherein the protein is phosphorylated.

109. The method of claim 107 wherein the protein is cysteinylated.

110. The method of claim 103 wherein the quantities of two or more post-translationally modified proteins which are general markers of ischemia are determined.

111. The method of any one of claims 97-110 wherein the quantity(ies) of the post-translationally modified protein(s) is(are) determined by a binding-partner assay.

112. The method of claim 111 wherein the binding-partner assay is an immunoassay.

113. The method of any one of claims 97-110 further comprising; obtaining one or more additional diagnostic parameters of placental ischemia; and using the quantity (ies) of the one or more post-translationally modified proteins and the additional diagnostic parameter(s) to diagnose or monitor the placental ischemia.

114. The method of claim 113 wherein the quantity(ies) of the post-translationally modified protein(s) is(are) determined by a binding-partner assay.

115. The method of claim 114 wherein the binding-partner assay is an immunoassay.

116. A method of diagnosing or monitoring ischemia in an animal comprising: (a) determining the quantity present in a body fluid of a phosphorylated protein

constituent of the body fluid; and (b) determining if the quantity of the phosphorylated protein is significantly altered compared to its level in the same body fluid from normal animals to determine if ischemia is present.

117. The method of claim 116 wherein the body fluid is serum or plasma.

118. The method of claim 116 wherein the phosphorylated protein is phosphorylated albumin.

119. The method of claim 116 wherein the ischemia is cardiac ischemia.

120. The method of claim 116 wherein the quantity of the phosphorylated protein is determined by a binding-partner assay.

121. The method of claim 120 wherein the binding-partner assay is an immunoassay.

122. The method of any one of claims 116-121 further comprising; obtaining one or more additional diagnostic parameters of ischemia; and using the quantity of phosphorylated protein and the additional diagnostic parameter(s) to diagnose or monitor the ischemia.

123. The method of claim 122 wherein the ischemia is cardiac ischemia and the additional diagnostic parameter is an electrocardiogram, a cardiac troponin I level, a cardiac troponin T level, or combinations of the foregoing.

124. A method of diagnosing or monitoring ischemia in an animal comprising: (a) determining the quantity present in a body fluid of a phosphorylated protein, wherein the phosphorylation of the protein occurred at least in part by substrate phosphorylation; and (b) determining if the quantity of the phosphorylated protein is significantly altered compared to its level in the same body fluid from normal animals to determine if ischemia is present.

125. The method of claim 124 wherein the body fluid is serum or plasma.

126. The method of claim 124 wherein the phosphorylated protein is phosphorylated albumin.

127. The method of claim 124 wherein the ischemia is cardiac ischemia.

128. The method of claim 127 wherein the phosphorylated protein is troponin I.

129. The method of claim 127 wherein the phosphorylated protein is troponin T.

130. The method of claim 124 wherein the quantity of the phosphorylated protein is determined by a binding-partner assay.

131. The method of claim 130 wherein the binding-partner assay is an immunoassay.

132. The method of any one of claims 124-131 further comprising; obtaining one or more additional diagnostic parameters of ischemia; and using the quantity of phosphorylated protein and the additional diagnostic parameter(s) to diagnose or monitor the ischemia.

133. The method of claim 132 wherein the ischemia is cardiac ischemia and the additional diagnostic parameter is an electrocardiogram, a cardiac troponin I

level, a cardiac troponin T level, or combinations of the foregoing.

134. A method of diagnosing or monitoring ischemia in an animal comprising: (a) determining the quantity of a cysteinylated protein present in a body fluid of the animal; and (b) determining if the quantity of the cysteinylated protein is significantly altered compared to its level in the same body fluid from normal animals to determine if ischemia is present.

135. The method of claim 134 wherein the body fluid is serum or plasma.

136. The method of claim 134 wherein the cysteinylated protein is cysteinylated albumin.

137. The method of claim 134 wherein the ischemia is cardiac ischemia.

138. The method of claim 134 wherein the ischemia is bowel ischemia.

139. The method of any one of claims 134-138 wherein the quantity of the cysteinylated protein is determined by a binding-partner assay.

140. The method of claim 139 wherein the binding-partner assay is an immunoassay.

141. The method of any one of claims 134-138 further comprising; obtaining one or more additional diagnostic parameters of ischemia; and using the quantity of the cysteinylated protein and the additional diagnostic parameter(s) to diagnose or monitor the ischemia.

142. The method of claim 141 wherein the quantity of the cysteinylated protein is determined by a binding-partner assay.

143. The method of claim 142 wherein the binding-partner assay is an immunoassay.

144. The method of claim 143 wherein the ischemia is cardiac ischemia and the additional diagnostic parameter is an electrocardiogram, a cardiac troponin I level, a cardiac troponin T level, or combinations of the foregoing.

145. A method of diagnosing or monitoring placental ischemia in a pregnant animal comprising: (a) determining the quantity of a cysteinylated protein present in a body fluid of the animal; and (b) determining if the quantity of the cysteinylated protein is significantly altered compared to its level in the same body fluid from normal pregnant animals to determine if placental ischemia is present.

146. The method of claim 145 wherein the body fluid is maternal serum or plasma.

147. The method of claim 145 wherein the cysteinylated protein is cysteinylated albumin.

148. The method of any one of claims 145-147 wherein the quantity of the cysteinylated protein is determined by a binding-partner assay.

149. The method of claim 148 wherein the binding-partner assay is an immunoassay.

150. The method of any one of claims 145-147 further comprising; obtaining one or more additional diagnostic parameters of placental ischemia; and using the quantity of the cysteinylated protein and the additional diagnostic parameter(s) to diagnose

or monitor the placental ischemia.

151. The method of claim 150 wherein the quantity of the cysteinylated protein is determined by a binding-partner assay.

152. The method of claim 151 wherein the binding-partner assay is an immunoassay.

153. A method of diagnosing, monitoring or predicting multiple organ failure in an animal comprising: (a) determining the quantity of a post-translationally modified protein present in a body fluid of the animal; and (b) determining if the quantity of the post-translationally modified protein is significantly altered compared to its level in the same body fluid from normal animals to determine if multiple organ failure is present or will develop.

154. The method of claim 153 wherein the body fluid is serum or plasma.

155. The method of claim 153 wherein the post-translationally-modified protein is a post-translationally modified albumin.

156. The method of claim 153 wherein the post-translationally-modified protein is a cysteinylated protein.

157. The method of claim 156 wherein the cysteinylated protein is cysteinylated albumin.

158. The method of any one of claims 153-157 wherein the quantity of the post-translationally-modified protein is determined by a binding-partner assay.

159. The method of claim 158 wherein the binding-partner assay is an immunoassay.

160. The method of any one of claims 153-157 further comprising; obtaining one or more additional diagnostic parameters of multiple organ failure; and using the quantity of the post-translationally-modified protein and the additional diagnostic parameter(s) to diagnose, monitor or predict the multiple organ failure.

161. The method of claim 160 wherein the quantity of the post-translationally-modified protein is determined by a binding-partner assay.

162. The method of claim 161 wherein the binding-partner assay is an immunoassay.

163. A binding partner specific for phosphorylated albumin.

164. A binding partner specific for a cysteinylated blood protein.

165. The binding partner of claim 164 which is specific for cysteinylated albumin.

166. A binding partner specific for a cysteinylated organ-specific or tissue-specific protein.

167. The binding partner of claim 166 which is specific for a cysteinylated heart-specific protein.

168. The binding partner of claim 167 which is specific for cysteinylated troponin I.

169. The binding partner of claim 167 which is specific for cysteinylated troponin T.

170. A binding partner specific for a post-translationally modified pregnancy-associated protein.

171. The binding partner of claim 170 which is specific for a cysteinylated pregnancy-associated protein.

172. The binding partner of claim 171 which is specific for cysteinylated .beta.-human chorionic gonadotropin, cysteinylated .alpha.-fetoprotein, cysteinylated pregnancy-associated protein 1A, cysteinylated erythropoietin or cysteinylated angiotensin.

173. The binding partner of claim 170 which is specific for a phosphorylated pregnancy-associated protein.

174. The binding partner of claim 173 which is specific for phosphorylated .beta.-human chorionic gonadotropin, phosphorylated .alpha.-fetoprotein, phosphorylated pregnancy-associated protein 1A, phosphorylated erythropoietin or phosphorylated angiotensin.

175. The binding partner of claim 165-174 which is an antibody.

176. The binding partner of claim 165-174 which is an aptamer.

177. A kit comprising: a container holding a binding partner specific for a post-translationally modified protein other than phosphorylated tau; and instructions directing that the binding partner is to be used to determine the quantity of the post-translationally modified protein present in a body fluid of an animal in order to diagnose or monitor inflammation.

178. The kit of claim 177 wherein the protein is a post-translationally protein which can be used to diagnose or monitor general inflammation.

179. The kit of claim 178 wherein the post-translationally-modified protein is a post-translationally modified albumin.

180. The kit of claim 179 wherein the post-translationally-modified albumin is phosphorylated albumin.

181. The kit of claim 179 wherein the post-translationally-modified albumin is cysteinylated albumin.

182. The kit of claim 177 wherein the post-translationally modified protein is a post-translationally-modified indicator protein.

183. The kit of claim 182 wherein the post-translationally modified indicator protein is a post-translationally-modified organ-specific or tissue-specific protein.

184. The kit of claim 182 wherein the post-translationally modified indicator protein is a post-translationally-modified disease-specific protein.

185. The kit of claim 177 wherein the post-translationally-modified protein is a phosphorylated protein

186. The kit of claim 177 wherein the post-translationally-modified protein is a cysteinylated protein.

187. The kit of any one of claims 177-186 further comprising one or more additional containers holding one or more additional binding partners specific for one or more additional post-translationally modified proteins, other than phosphorylated tau, and the instructions direct that the additional binding partner(s) is(are) to be used to determine the quantity(ies) of the one or more additional post-translationally modified protein(s) present in one or more body fluids of an animal in order to diagnose or monitor inflammation.

188. The kit of any one of claims 177-186 wherein the binding partner(s) is(are) antibodies.

189. The kit of claim 187 wherein the binding partners are antibodies.

190. The kit of any one of claims 177-186 wherein the binding partner(s) is(are) aptamers.

191. The kit of claim 187 wherein the binding partners are aptamers.

192. A kit comprising: a container holding a binding partner specific for a post-translationally modified organ-specific or tissue-specific protein, other than phosphorylated tau; and instructions directing that the binding partner is to be used to determine the quantity of the post-translationally modified protein present in a body fluid of an animal in such a manner that the protein is not denatured prior to the determination in order to diagnose or monitor ischemia of the organ or tissue.

193. The kit of claim 192 wherein the post-translationally-modified protein is a phosphorylated protein.

194. The kit of claim 192 wherein the post-translationally-modified protein is a cysteinylated protein.

195. The kit of claim 192 wherein the post-translationally-modified protein is a post-translationally modified heart-specific protein.

196. The kit of claim 195 wherein the post-translationally-modified heart-specific protein is a post-translationally modified troponin I.

197. The kit of claim 196 wherein the post-translationally-modified troponin I is phosphorylated troponin I.

198. The kit of claim 196 wherein the post-translationally-modified troponin I is cysteinylated troponin I.

199. The kit of claim 195 wherein the post-translationally-modified heart-specific protein is a post-translationally modified troponin T.

200. The kit of claim 199 wherein the post-translationally-modified troponin T is phosphorylated troponin T.

201. The kit of claim 199 wherein the post-translationally-modified troponin T is cysteinylated troponin T.

202. The kit of any one of claims 192-201 further comprising one or more additional containers holding one or more additional binding partners specific for one or more additional post-translationally modified proteins, and the instructions direct that the additional binding partner(s) is(are) to be used to determine the quantity(ies) of the one or more additional post-translationally modified protein(s) present in a body fluid of an animal in such a manner that the protein is not denatured prior to the determination in order to diagnose or monitor ischemia of the organ or tissue.

203. The kit of any one of claims 192-201 wherein the binding partner(s) is(are) antibodies.

204. The kit of claim 202 wherein the binding partners are antibodies.

205. The kit of any one of claims 192-201 wherein the binding partner(s) is(are) aptamers.

206. The kit of claim 202 wherein the binding partners are aptamers.

207. A kit comprising: a container holding a binding partner specific for a post-translationally modified pregnancy-associated protein; and instructions directing that the binding partner is to be used to determine the quantity of the post-translationally modified protein present in a body fluid of a pregnant animal in order to diagnose or monitor placental ischemia.

208. The kit of claim 207 wherein the post-translationally modified pregnancy-associated protein is a cysteinylated protein.

209. The kit of claim 207 wherein the post-translationally modified pregnancy-associated protein is a phosphorylated protein.

210. The kit of claim 207 wherein the post-translationally modified pregnancy-associated protein is a post-translationally modified .beta.-human chorionic gonadotropin, .alpha.-fetoprotein, pregnancy-associated protein 1A, erythropoietin, angiotensin, or combinations of the foregoing.

211. The kit of claim 210 wherein the post-translationally modified pregnancy-associated protein is a cysteinylated modified i-human chorionic gonadotropin, .alpha.-fetoprotein, pregnancy-associated protein 1A, erythropoietin, angiotensin, or combinations of the foregoing.

212. The kit of claim 210 wherein the post-translationally modified pregnancy-associated protein is a phosphorylated modified i-human chorionic gonadotropin, .alpha.-fetoprotein, pregnancy-associated protein 1A, erythropoietin, angiotensin, or combinations of the foregoing.

213. The kit of claims 207 further comprising one or more additional containers holding one or more additional binding partners specific for one or more additional post-translationally modified proteins, and the instructions direct that the additional binding partner(s) is(are) to be used to determine the quantity(ies) of the one or more additional post-translationally modified protein(s) present in a body fluid of a pregnant animal in order to diagnose or monitor placental ischemia.

214. The kit of any one of claims 207-213 wherein the binding partner is an antibody.

215. The kit of any one of claims 205-213 wherein the binding partner is an aptamer.

216. A kit comprising: a container holding a binding partner specific for a phosphorylated protein constituent of a body fluid; and instructions directing that the binding partner is to be used to determine the quantity of the phosphorylated protein present in a body fluid of an animal in order to diagnose or monitor ischemia.

217. The kit of claim 216 wherein the phosphorylated protein is phosphorylated albumin.

218. The kit of claims 216 further comprising one or more additional containers holding one or more additional binding partners specific for one or more additional post-translationally modified proteins, and the instructions direct that the additional binding partner(s) is(are) to be used to determine the quantity(ies) of the one or more additional post-translationally modified protein(s) present in a body fluid of an animal in order to diagnose or monitor ischemia.

219. The kit of claim 216, 217 or 218 wherein the binding partner is an antibody.

220. The kit of claim 216, 217 or 218 wherein the binding partner is an aptamer.

221. A kit comprising: a container holding a binding partner specific for a cysteinylated protein; and instructions directing that the binding partner is to be used to determine the quantity of the cysteinylated protein present in a body fluid of an animal in order to diagnose or monitor ischemia.

222. The kit of claim 221 wherein the cysteinylated protein is cysteinylated albumin.

223. The kit of claims 221 further comprising one or more additional containers holding one or more additional binding partners specific for one or more additional post-translationally modified proteins, and the instructions direct that the additional binding partner(s) is(are) to be used to determine the quantity(ies) of the one or more additional post-translationally modified protein(s) present in a body fluid of an animal in order to diagnose or monitor ischemia.

224. The kit of claim 221, 222 or 223 wherein the binding partner is an antibody.

225. The kit of claim 221, 222 or 223 wherein the binding partner is an aptamer.

226. A kit comprising: a container holding a binding partner specific for a cysteinylated protein; and instructions directing that the binding partner is to be used to determine the quantity of the cysteinylated protein present in a body fluid of a pregnant animal in order to diagnose or monitor placental ischemia.

227. The kit of claim 226 wherein the cysteinylated protein is cysteinylated albumin.

228. The kit of claims 226 further comprising one or more additional containers holding one or more additional binding partners specific for one or more additional post-translationally modified proteins, and the instructions direct that the additional binding partner(s) is(are) to be used to determine the quantity(ies) of the one or more additional post-translationally modified protein(s) present in a body fluid of a pregnant animal in order to diagnose or monitor placental ischemia.

229. The kit of claim 226, 227 or 228 wherein the binding partner is an antibody.

230. The kit of claim 226, 227 or 228 wherein the binding partner is an aptamer.

231. A kit comprising: a container holding a binding partner specific for a post-translationally modified protein; and instructions directing that the binding partner is to be used to determine the quantity of the post-translationally modified protein present in a body fluid of an animal in order to diagnose, monitor or predict multiple organ failure.

232. The kit of claim 231 wherein the post-translationally modified protein is a cysteinylated protein.

233. The kit of claim 232 wherein the cysteinylated protein is cysteinylated albumin.

234. The kit of claim 231 further comprising one or more additional containers holding one or more additional binding partners specific for one or more additional post-translationally modified proteins, and the instructions direct that the additional binding partner(s) is(are) to be used to determine the quantity(ies) of the one or more additional post-translationally modified protein(s) present in a body fluid of an animal in order to diagnose, monitor or predict multiple organ failure.

235. The kit of any one of claims 231-234 wherein the binding partner is an antibody.

236. The kit of any one of claims 231-234 wherein the binding partner is an aptamer.

237. A kit comprising: a container holding a binding partner specific for a phosphorylated protein other than phosphorylated tau; and a container holding a phosphatase inhibitor or a mixture of phosphatase inhibitors.

238. The kit of claim 237 further comprising one or more additional containers holding one or more additional binding partners specific for one or more additional post-translationally modified proteins.

239. The kit of claim 237 or 238 wherein the binding partner is an antibody.

240. The kit of claim 237 or 238 wherein the binding partner is an aptamer.

241. A method of diagnosing appendicitis in an animal comprising the following steps: (a) obtaining a first body fluid from the animal and obtaining a second body fluid from the animal, wherein the first and second body fluids may be the same or different; (b) determining if the quantity of orthohydroxyhippuric acid (OHHA) present in the first body fluid of the animal is significantly elevated compared to its level in the same body fluid from normal animals; (c) determining if the quantity of a marker of general inflammation present in the second body fluid of the animal is significantly altered compared to its level in the same body fluid from normal animals; and (d) correlating the results obtained in steps (b) and (c) to the presence or absence of appendicitis.

242. The method of claim 241 wherein the first body fluid is urine.

243. The method of claim 242 wherein step (b) comprises: mixing a portion of the urine from the animal being diagnosed with a color-producing reagent that produces a color when it is contacted with OHHA; incubating the urine and the color-producing reagent for a time sufficient to allow production of the color; and

comparing the color produced to a color comparison chart or to the colors produced by standards comprising known amounts of OHHA to determine if the quantity of OHHA present in the urine is significantly elevated.

244. The method of claim 243 wherein the color-producing reagent is ferric ions bonded to silica.

245. The method of claim 241 wherein step (b) is performed using a binding partner assay.

246. The method of claim 241 wherein step (c) is performed using a binding partner assay.

247. The method of claim 241 wherein the second body fluid is urine.

248. The method of claim 247 wherein the marker of general inflammation is interleukin 8.

249. The method of claim 241 wherein the second body fluid is serum or plasma.

250. The method of claim 249 wherein the marker of general inflammation is leukocyte count.

251. The method of claim 249 wherein the marker of general inflammation is neutrophil band count.

252. The method of claim 241 wherein the marker of general inflammation is a post-translationally modified protein.

253. The method of claim 249 wherein the marker of general inflammation is a post-translationally modified protein

254. The method of claim 253 wherein the post-translationally modified protein is phosphorylated albumin.

255. The method of claim 253 wherein the post-translationally modified protein is cysteinylated albumin.

256. The method of any one of claims 241-255 wherein the animal is a human.

257. A kit for diagnosing appendicitis comprising Parts (A) and (B), wherein: Part (A) comprises at least one container holding a reagent useful for determining if the quantity of orthohydroxyhippuric acid (OHHA) present in a body fluid of an animal is significantly elevated compared to its level in the same body fluid from normal animals; and Part (B) comprises at least one container holding a reagent useful for determining if the quantity of a marker of general inflammation present in a body fluid of the animal is significantly altered compared to its level in the same body fluid from normal animals.

258. The kit of claim 257 wherein Part (A) comprises a container holding a color-producing reagent that produces a color when contacted with OHHA.

259. The kit of claim 258 wherein the color-producing reagent is ferric ions bonded to silica.

260. The kit of claim 258 or 259 further comprising a color comparison chart.

261. The kit of claim 258 or 259 further comprising one or more containers holding standards comprising known amounts of OHHA.

262. The kit of claim 257 wherein Part (A) comprises a container holding a binding partner specific for OHHA.

263. The kit of claim 257 wherein Part (B) comprises a container holding a binding partner specific for a post-translationally modified protein.

264. The kit of claim 263 wherein the post-translationally modified protein is phosphorylated albumin.

265. The kit of claim 263 wherein the post-translationally modified protein is cysteinylated albumin.

266. The kit of claim 257 wherein Part (B) comprises a container holding a binding partner specific for a cytokine.

267. The kit of claim 266 wherein the cytokine is interleukin 8.

268. A kit for diagnosing appendicitis comprising: at least one container holding a reagent useful for determining if the quantity of marker of general inflammation present in a body fluid of an animal is significantly altered compared to its level in the same body fluid from normal animals; and instructions directing how the reagent is to be used to diagnose appendicitis.

269. The kit of claim 268 wherein the reagent is a binding partner specific for a marker of general inflammation.

270. The kit of claim 269 comprising a container holding a binding partner specific for a post-translationally modified protein.

271. The kit of claim 270 wherein the post-translationally modified protein is phosphorylated albumin.

272. The kit of claim 270 wherein the post-translationally modified protein is cysteinylated albumin.

273. The kit of claim 269 comprising a container holding a binding partner specific for a cytokine.

274. The kit of claim 273 wherein the cytokine is interleukin 8.

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L9: Entry 3 of 21 File: PGPB Oct 21, 2004

PGPUB-DOCUMENT-NUMBER: 20040209379
PGPUB-FILING-TYPE: new
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TITLE: Diagnosis and monitoring of diseases

PUBLICATION-DATE: October 21, 2004

INVENTOR-INFORMATION:

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US-CL-CURRENT: 436/86

CLAIMS:

We claim:

1. A method for diagnosing or monitoring a disease or condition comprising the steps of: (a) obtaining a biological sample from a patient to be diagnosed or monitored; (b) determining the quantity of a target marker in said biological sample, wherein said target marker is: (i) a truncated disease-associated protein lacking its two N-terminal amino acids, wherein said truncated disease-associated protein is not human serum albumin; (ii) a truncated disease-associated protein lacking its two C-terminal amino acids; (iii) a truncated disease-associated protein lacking its two N-terminal amino acids and its two C-terminal amino acids; (iv) a diketopiperazine (DKP) comprising the two N-terminal amino acids of a disease-associated protein; or (v) a DKP comprising the two C-terminal amino acids of a disease-associated protein; or (vi) two or more target markers selected from those listed in (i) through (v) above; provided that when only a single DKP is used as the marker, it will not be His-Pro DKP; and (c) determining if the quantity(ies) of said target marker(s) in said biological sample is(are) indicative of the presence, absence or status of the disease or condition.

2. The method of claim 1, wherein said marker is a truncated disease-associated protein.

3. The method of claim 1, wherein said marker is X-Y-DKP, wherein X-Y-DKP is a diketopiperazine composed of amino acids X and Y, and X and Y are the two N-terminal or the two C-terminal amino acids of a disease-associated protein.

4. The method of claim 3, wherein X and Y are the two C-terminal amino acids of a disease-associated protein.

5. The method of claim 4, wherein X-Y-DKP is Arg-Arg-DKP, Gln-Asn-DKP, Lys-Arg-DKP, Glu-Phe-DKP, Ser-Met-DKP, Cys-Asn-DKP, Lys-Ala-DKP, Gln-Asn-DKP, Gly-Leu-DKP, Ala-Ala-DKP, Trp-Pro-DKP, Asn-Ser-DKP, Leu-Pro-DKP, Asp-Arg-DKP, His-Gly-DKP, Gln-Gly-

DKP, Glu-Ser-DKP, Asn-Pro-DKP, Lys-Leu-DKP, Pro-Cys-DKP, Asn-Lys-DKP, Asp-Arg-DKP, Ala-Pro-DKP, Arg-His-DKP or combinations of the foregoing.

6. The method of claim 3, wherein X and Y are the two N-terminal amino acids of a disease-associated protein.

7. The method of claim 6, wherein X-Y-DKP is N-acetyl-Ala-Ser-DKP, N-acetyl-Ala-phosphorylated-Ser-DKP, Asp-Ala-DKP, Glu-Ile-DKP, Glu-Val-DKP, Phe-Pro-DKP, Ala-Glu-DKP, Phe-Val-DKP, Gly-Ile-DKP, Met-Ala-DKP, Met-Asp-DKP, Glu-Lys-DKP, Gln-Thr-DKP, Ala-Val-DKP, Gly-Leu-DKP, Ala-Pro-DKP, Glu-Ala-DKP, Pro-Glu-DKP, Lys-Ser-DKP, Ile-Val-DKP, Gln-Tyr-DKP, Lys-Glu-DKP, Glu-Asp-DKP, Ala-Pro-DKP, Ala-Asn-DKP, Ala-Leu-DKP, Ser-Leu-DKP, Val-Leu-DKP, Val-His-DKP, Gly-His-DKP, His-Pro-DKP, Ser-Pro-DKP or combinations of the foregoing.

8. The method of claim 3, wherein X-Y-DKP is N-acetyl-Ala-Ser-DKP, N-acetyl-Ala-phosphorylated-Ser-DKP, Asp-Ala-DKP, Arg-Arg-DKP, Gln-Asn-DKP or combinations of the foregoing.

9. The method of claim 3, wherein X-Y-DKP is Asp-Ala-DKP, Met-Ala-DKP, Gln-Asn-DKP, Gly-Leu-DKP or combinations of the foregoing.

10. The method of claim 3, wherein X-Y-DKP is Gly-Leu-DKP, Ala-Pro-DKP, Glu-Ala-DKP, Leu-Pro-DKP, Asp-Arg-DKP, His-Gly-DKP or combinations of the foregoing.

11. The method of claim 3, wherein X-Y-DKP is Arg-His-DKP, His-Pro-DKP, Ser-Pro-DKP, or combinations of the foregoing.

12. The method of claim 3, wherein X-Y-DKP is Gly-Leu-DKP, Pro-Glu-DKP, Gln-Gly-DKP, Glu-Ser-DKP, or combinations of the foregoing.

13. The method of any one of claims 1-3, wherein said disease-associated protein is myelin basic protein, beta-amyloid, Rh factor, pulmonary surfactant-associated protein A, B or D, insulin, tau protein, alpha-synuclein, albumin, C-reactive protein, interleukin 8, S100 proteins, beta-chorionic gonadotropin, fetal erythropoietin, pregnancy-associated protein A, myoglobin, troponin I, troponin T, prostate specific antigen, amylase, lipase, alphal-antitrypsyn, erthyropoietin, activated protein C, tethal chain, zeta chain, alpha chain, beta chain, delta chain, epsilon chain, gamma AG and brain natriuretic peptide.

14. The method of any one of claims 1-3, wherein the disease or condition is multiple sclerosis, rheumatoid arthritis, acute respiratory distress syndrome, cystic fibrosis, diabetes mellitus, Alzheimer's disease, Parkinson's disease, inflammation, ischemia, cerebral ischemia, placental ischemia, myocardial infarction, prostate cancer, pancreatitis, emphysema, renal disease, cancer, chemotherapy, hemoglobinopathies, anemnias or congestive heart failure.

15. The method of claim 1, wherein two or more target markers are quantitated.

16. A method of diagnosing or monitoring multiple sclerosis (MS) in a patient, comprising the steps of: (a) obtaining a biological sample from said patient; (b) measuring the amount of a MS diagnostic compound in said biological sample to diagnose or monitor said MS in said patient.

17. The method of claim 16, wherein said MS diagnostic compound is: (i) a compound having a mass of about 175 as determined by liquid chromatography and mass spectrometry; (ii) a compound having a mass of about 145 as determined by liquid chromatography and mass spectrometry; (iii) Asp-Ala diketopiperazine (DA-DKP); (iv)

N-acetyl-alanine-serine diketopiperazine (NAS-DKP); or (v) combinations of the foregoing; wherein: the absence of compounds (i) and/or (ii) or an elevated amount of DA-DKP and/or NAS-DKP in said biological sample is indicative of MS; and an elevated amount of DA-DKP and/or NAS-DKP in said biological sample is indicative of active MS.

18. The method of claim 17, wherein said MS is active MS.

19. The method of claim 18, wherein said MS diagnostic compound is DA-DKP, NAS-DKP or both.

20. A method of diagnosing or monitoring Alzheimer's disease in a patient, comprising the steps of: (a) obtaining a biological sample from said patient; and (b) measuring the amount of an Alzheimer's diagnostic compound in said biological sample to diagnose or monitor said Alzheimer's disease.

21. The method of claim 20, wherein said Alzheimer's diagnostic compound is: (i) a compound having a mass of about 175 as determined by liquid chromatography and mass spectrometry; (ii) Asp-Ala-DKP; or (iii) both (i) and (ii).

22. A method of diagnosing or monitoring placental ischemia in a pregnant patient, comprising the steps of: (a) obtaining a biological sample from said patient; and (b) measuring the amount of a placental ischemia diagnostic compound in said biological sample to diagnose or monitor said placental ischemia.

23. The method of claim 22, wherein said placental ischemia diagnostic compound is: (i) Gly-Leu-DKP; (ii) Ala-Pro-DKP; or (iii) both Gly-Leu-DKP and Ala-Pro-DKP.

24. The method of claim 1, 16, 20 or 22, wherein step (b) is conducted by mass spectrometry, chemical assay or immunoassay.

25. The method of claim 24, wherein step (b) is conducted by immunoassay.

26. The method of claim 25, wherein said immunoassay is conducted by using one or more binding partners specific for a target marker, MS diagnostic compound, Alzheimer's diagnostic compound or placental ischemia diagnostic compound.

27. The method of claim 26, wherein the binding partner is an antibody or an aptamer.

28. The method of claims 1, 16, 20 or 22, wherein said biological sample is a body fluid.

29. The method of claim 28, wherein said body fluid is serum, plasma, blood, urine, saliva, cerebrospinal fluid, tears, semen, vaginal secretion, amniotic fluid or cord blood.

30. The method of claim 29, wherein said body fluid is plasma or serum.

31. The method of claims 1, 16, 20 or 22, wherein said patient is an animal.

32. The method of claims 31, wherein said patient is a human.

33. An isolated binding partner having specificity for a target marker selected from the group consisting of: (a) a truncated disease-associated protein lacking its two N-terminal amino acids, wherein said truncated disease-associated protein

is not human serum albumin; (b) a truncated disease-associated protein lacking its two C-terminal amino acids; (c) a truncated disease-associated protein lacking its two N-terminal amino acids and its two C-terminal amino acids; (d) a diketopiperazine (DKP) comprising the two N-terminal amino acids of a disease-associated protein, wherein the DKP is not His-Pro DKP; and (e) a DKP comprising the two C-terminal amino acids of a disease-associated protein, wherein the DKP is not His-Pro DKP.

34. The isolated binding partner of claim 33, wherein the binding partner has specificity for a DKP.

35. The isolated binding partner of claim 34, wherein the binding partner has specificity for Arg-Arg-DKP, Gln-Asn-DKP, Lys-Arg-DKP, Glu-Phe-DKP, Ser-Met-DKP, Cys-Asn-DKP, Lys-Ala-DKP, Gln-Asn-DKP, Gly-Leu-DKP, Ala-Ala-DKP, Trp-Pro-DKP, Asn-Ser-DKP, Leu-Pro-DKP, Asp-Arg-DKP, His-Gly-DKP, Gln-Gly-DKP, Glu-Ser-DKP, Asn-Pro-DKP, Lys-Leu-DKP, Pro-Cys-DKP, Asn-Lys-DKP, Asp-Arg-DKP, Ala-Pro-DKP or Arg-His-DKP.

36. The isolated binding partner of claim 34, wherein the binding partner has specificity for N-acetyl-Ala-Ser-DKP, N-acetyl-Ala-phosphorylated-Ser- -DKP, Asp-Ala-DKP, Glu-Ile-DKP, Glu-Val-DKP, Phe-Pro-DKP, Ala-Glu-DKP, Phe-Val-DKP, Gly-Ile-DKP, Met-Ala-DKP, Met-Asp-DKP, Glu-Lys-DKP, Gln-Thr-DKP, Ala-Val-DKP, Gly-Leu-DKP, Ala-Pro-DKP, Glu-Ala-DKP, Pro-Glu-DKP, Lys-Ser-DKP, Ile-Val-DKP, Gln-Tyr-DKP, Lys-Glu-DKP, Glu-Asp-DKP, Ala-Pro-DKP, Ala-Asn-DKP, Ala-Leu-DKP, Ser-Leu-DKP, Val-Leu-DKP, Val-His-DKP, Gly-His-DKP, His-Pro-DKP or Ser-Pro-DKP.

37. The isolated binding partner of any one of claims 33-36, wherein said binding partner is an antibody.

38. The isolated binding partner of claim 35, wherein said antibody is a monoclonal antibody.

39. The isolated binding partner of any one of claims 33-36, wherein said binding partner is an aptamer.

40. A composition comprising the binding partner of any one of claims 33-39 in a physiologically-acceptable carrier.

41. A kit comprising the binding partner of claim 33 and associated reagents for quantitating the target marker.

42. A kit comprising the binding partner of any one of claims 34-36 and associated reagents for quantitating the DKP.

43. The kit of claim 41 or 42, wherein said binding partner is an antibody.

44. The kit of claim 43, wherein said antibody is a monoclonal antibody.

45. The kit of claim 41 or 42, wherein said binding partner is an aptamer.

46. The kit of claim 41 or 42, wherein said binding partner is specific for a MS diagnostic compound, an Alzheimer's diagnostic compound or a placental ischemia diagnostic compound.

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L9: Entry 2 of 21 File: PGPB Jan 27, 2005

PGPUB-DOCUMENT-NUMBER: 20050021235
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DOCUMENT-IDENTIFIER: US 20050021235 A1

TITLE: Method and system for optically performing an assay to determine a medical condition

PUBLICATION-DATE: January 27, 2005

INVENTOR-INFORMATION:

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US-CL-CURRENT: 702/19

CLAIMS:

What is claimed is:

1. A method for detecting a medical condition comprising: providing a patient fluid sample divided into first and second portions, and combining a substance for providing free metal ions with the first portion of the sample; irradiating both the first and second portions of the sample with light; determining absorbance values for the first and second portions; obtaining a differential absorbance value from the first and second portions; analyzing the differential absorbance value for determining one or more characteristics that are indicative of whether the medical condition is present; wherein said analyzing step uses principal component analysis for reducing a dimension of the differential absorbance value.

2. The method of claim 1, wherein the medical condition is ischemia.

3. The method of claim 1, wherein the metal ion is cobalt ion.

4. A method of diagnosing an ischemic event comprising: a) providing a first and second patient sample comprising albumin; b) adding to the first patient sample a metal ion, whereby the metal ion binds to the albumin; c) conducting optical analyses of the first and second patient samples to generate signals or spectra, respectively; d) measuring the amount of metal bound to the albumin by comparing the signals or spectra of step (c) to generate a differential signal or spectra; and e) comparing the differential signal or spectra to a standard curve or mathematical model that correlates the differential signal or spectra to amount of metal bound to albumin, whereby an ischemic event may be diagnosed if the measured amount of metal bound to albumin is below a defined value.

5. The method of claim 4, wherein the patient samples are serum.

6. The method of claim 4, wherein the first and second patient samples are provided by dividing an original patient sample.

7. The method of claim 43, wherein the metal ion is cobalt ion.

8. The method of claim 4, wherein the metal ion binds to the N-terminus of the albumin.

9. The method of claim 4, wherein the optical analyses are absorbance spectroscopy and the analyses is conducted in the range of 300-450 nm.

10. The method of claim 4, wherein the optical analyses comprise fluorescence spectroscopy, said method further comprising: adding to the first patient sample a fluorescent dye in step (b), wherein the dye binds to said metal ion and wherein the fluorescence signal changes as a function of whether the metal ion is unbound or bound to the albumin.

11. The method of claim 4, further comprising: analyzing the differential signal or spectra of step (d) using principal component analysis.

12. A method for diagnosing an ischemic event, comprising: a) adding a metal ion and a fluorescent dye to a patient sample comprising albumin, whereby the dye binds to the metal ion which may bind to the albumin; b) measuring the metal bound to the albumin by measuring a fluorescent signal of the sample, wherein the fluorescent signal changes as a function of whether the metal ion is unbound or bound to the albumin; and c) comparing the fluorescent signal to a standard curve or mathematical model that correlates the fluorescent signal to an amount of metal ion bound to albumin, whereby the measurement of metal ion bound to albumin below a defined value may be diagnostic for an ischemic event.

13. The method of claim 12 wherein the metal ion and fluorescent dye are added as a conjugate.

14. The method of claim 12, wherein the fluorescent signal is quenched or shifts to a different wavelength when the dye is bound to a metal ion that is bound to the albumin.

15. The method of claim 12, wherein the metal ion is a cobalt ion.

16. The method of claim 12, wherein the fluorescent dye is selected from the group consisting of Cumarin, Rhodamine and Newport green.

17. A method of rapidly diagnosing an ischemic event comprising: a) providing a first and second patient sample comprising albumin; b) adding to the first patient sample a metal ion, whereby the metal ion binds to the albumin in a reaction that reaches equilibrium at a predetermined time; c) conducting, during a defined time interval prior to achievement of equilibrium, optical analyses of the first and second patient samples to generate first and second signals or spectra, respectively, for each sample at selected time points during the defined time interval; d) measuring the rate of change of amount of metal bound to the albumin over the defined time interval by comparing the first and second signals or spectra for each time point to generate differential signals or spectra for each time point in the time interval; e) calculating a rate of change in the differential signals or spectra over the time interval; f) and comparing the rate of change of signal or spectra to a standard curve or mathematical model that correlates rate of change with projected metal bound to albumin at equilibrium, whereby an ischemic event may be diagnosed if the projected amount of metal bound to albumin is below a defined

value.

18. A method of rapidly diagnosing an ischemic event, comprising: a) adding a metal ion and a fluorescent dye to a patient sample comprising albumin, whereby the dye binds to the metal ion which binds to the albumin in a reaction that reaches equilibrium at a predetermined time, wherein the fluorescent dye's signal changes as a function of whether the metal ion is unbound or bound to the albumin; b) measuring the rate of change of metal bound to the albumin by measuring the fluorescent signal of the sample at selected time points over a time interval that is prior to achievement of equilibrium; c) calculating the rate of change of the fluorescent signal over the time interval; and d) comparing the rate of change of the fluorescent signal to a standard curve or mathematical model that correlates the rate of change in fluorescent signal to a projected amount of metal ion bound to albumin at equilibrium, whereby ischemia may be diagnosed if the measured rate of change of metal ion bound to albumin is below a defined value.

19. A method for diagnosing an ischemic event comprising: (a) providing a patient sample comprising albumin, a portion of which may be N-terminally modified; (b) measuring the N-terminally modified albumin by measuring absorbance of the sample, and comparing the absorbance to a standard curve or mathematical model that correlates the absorbance to a ratio of modified to unmodified albumin, wherein an ischemic event may be diagnosed if the ratio is below a defined value.

20. The method of claim 19, wherein the patient sample comprises whole blood, serum or plasma provided in a sample container and the absorbance is measured with a spectral probe placed in the sample.

21. The method of claim 19, wherein the patient sample comprises whole blood in the patient's blood vessel and the absorbance is measured with a spectral probe placed in the blood vessel.

22. An instrument for detecting a medical condition, comprising: a spectral probe having a tip for insertion into a patient fluid sample and receiving spectral light from the patient fluid sample; a spectrophotometer coupled to said spectral probe for quantifying each frequency of spectral light received by said spectral probe and outputting a signal representative of the quantity of each frequency of spectral light; a computing unit, comprising: an input coupled to receive the signal from said spectrophotometer; a memory for storing a model representing spectral light data obtained from a first set of patients known to have the medical condition and a second set of individuals known to not have the medical condition, whereby the model includes a value identified with a high probability of the presence of the medical condition; a processor programmed to execute instructions for: comparing the quantity of each frequency of spectral light from the patient with corresponding data in the stored model; and determining whether the quantity of each frequency of spectral light is indicative of the presence of the medical condition in the patient; and an output to provide the determination to a user.

23. A method for providing an instrument for diagnosing a medical condition in a patient, comprising: obtaining a control fluid sample from a first plurality of control individuals known to have the medical condition; obtaining a control fluid sample from a second plurality of control individuals known to not have the medical condition; dividing each control fluid sample into first and second portions; combining a substance for providing free metal ions with the first portion of each control fluid sample; irradiating both the first and second portions of each control fluid sample with light; determining absorbance values for the first and second portions of each control fluid sample; obtaining a differential absorbance value from the first and second portions of each control fluid sample; generating a principal component analysis model of the obtained differential absorbance values,

the principal component analysis model including a value indicative of the presence of the medical condition; storing the generated principal component analysis model in a computer readable format; providing computer executable instructions for: providing a differential absorbance value, determined from first and second portions of a patient fluid sample obtained from a patient, said first portion having been combined with free metal ions, and comparing said differential value with the stored principal component analysis model; in response to the comparing step, determining whether the differential absorbance value of the patient fluid sample is indicative of the presence of the medical condition.

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☐ 1. Document ID: US 6815210 B1

L5: Entry 1 of 4 File: USPT Nov 9, 2004

US-PAT-NO: 6815210
DOCUMENT-IDENTIFIER: US 6815210 B1

TITLE: Total protein detection methods and devices

DATE-ISSUED: November 9, 2004

INVENTOR-INFORMATION:

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US-CL-CURRENT: 436/86; 422/55, 422/56, 436/169

Full | Title | Citation | Front | Review | Classification | Date | Reference | | | Claims | KWIC | Draw De

☐ 2. Document ID: US 5876944 A

L5: Entry 2 of 4 File: USPT Mar 2, 1999

US-PAT-NO: 5876944
DOCUMENT-IDENTIFIER: US 5876944 A

TITLE: Method for amplification of the response signal in a sandwich immunoassay

DATE-ISSUED: March 2, 1999

INVENTOR-INFORMATION:

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US-CL-CURRENT: 435/7.1; 422/56, 422/60, 436/170, 436/510, 436/65, 436/814, 436/88

Full | Title | Citation | Front | Review | Classification | Date | Reference | | | Claims | KWIC | Draw De

☐ 3. Document ID: US 5593895 A

L5: Entry 3 of 4 File: USPT Jan 14, 1997

US-PAT-NO: 5593895
DOCUMENT-IDENTIFIER: US 5593895 A

TITLE: Method for the detection of protein in urine

DATE-ISSUED: January 14, 1997

INVENTOR-INFORMATION:

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US-CL-CURRENT: 436/86; 422/56, 435/287.7, 436/169

Full | Title | Citation | Front | Review | Classification | Date | Reference | | | Claims | KWIC | Draw De

☐ 4. Document ID: US 5326707 A

L5: Entry 4 of 4 File: USPT Jul 5, 1994

US-PAT-NO: 5326707
DOCUMENT-IDENTIFIER: US 5326707 A

TITLE: Composition and device for urinary protein assay and method of using the same

DATE-ISSUED: July 5, 1994

INVENTOR-INFORMATION:

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US-CL-CURRENT: 436/86; 252/408.1, 422/56, 436/87, 436/88

Full | Title | Citation | Front | Review | Classification | Date | Reference | | | Claims | KWIC | Draw De

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L6: Entry 1 of 1 File: USPT Jul 27, 2004

US-PAT-NO: 6767708
DOCUMENT-IDENTIFIER: US 6767708 B1

TITLE: Stabilized aqueous steroid immunoassay standards

DATE-ISSUED: July 27, 2004

INVENTOR-INFORMATION:

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US-CL-CURRENT: 435/7.1; 435/7.93, 435/963, 435/967, 436/13, 436/817, 436/826

CLAIMS:

We claim:

1. A calibrator composition for use as a reference standard in an immunoassay consisting essentially of a steroid and diethylene triamine pentaacetic acid in an aqueous medium.

2. The composition of claim 1, wherein said aqueous medium is a protein containing aqueous medium.

3. An aqueous steroid calibrator solution for use as a reference standard in an immunoassay consisting essentially of: 1) a steroid compound capable of undergoing transition metal catalyzed oxidative degradation in an aqueous medium; 2) diethylenetriamine pentaacetic acid; and 3) a protein.

4. The composition of claim 3 wherein said steroid is present in a concentration between about 2.5.times.10.sup.-11 and 1.0.times.10.sup.-7 g/ml.

5. The composition of claim 3, wherein said diethylenetriamine pentaacetic acid is present in a concentration of greater than about 0.1 mM.

6. The composition of claim 5 wherein said diethylenetriamine pentaacetic acid is present in a concentration between about 0.2 and 50 mM.

7. A steroid containing aqueous calibrator solution for use as reference standard in an immunoassay consisting essentially of: 1) a steroid compound capable of undergoing transition metal catalyzed oxidative degradation in an aqueous medium; 2) diethylenetriamine pentaacetic acid; and 3) a protein in a

range between about 10 mg/mL to 300 mg/mL.

8. The composition of claim 7, wherein said solution is buffered.

9. The composition of claim 7 wherein said protein is bovine serum albumin.

10. The composition of claim 7 wherein the protein is charcoal stripped normal human serum.

11. The composition of claim 7 wherein said steroid compound is estradiol or progesterone.

12. The composition of claim 11 wherein the steroid compound is estradiol.

13. The composition of claim 12 wherein said steroid is estradiol and said protein is steroid free bovine serum albumin.

14. The composition of claim 13 wherein said aqueous solution is other than plasma.

15. The composition of claim 11 wherein said diethylenetriamine pentaacetic acid is present in a concentration of greater than about 0.1 mM.

16. The composition of claim 15 wherein said diethylenetriamine pentaacetic acid is present in a concentration between about 0.2 and 50 mM.

17. The composition of claim 7 herein said steroid is present in a concentration between about 2.5.times.10.sup.-11 and 1.0.times.10.sup.-7 g/ml.

18. A method for stabilizing aqueous metal-ion containing solutions of steroid immunoassay reference standards comprising the step of adding an effective chelating amount of at least about 0.1 mM of diethylene triamine pentaacetic acid to a steroid in said aqueous solution, wherein said acid sequesters metal ions from said solution.

19. The method of claim 18 wherein the chelating amount of diethylene triamine pentaacetic acid is from about 0.2 mM to 50 mM.

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L5: Entry 4 of 4 File: USPT Jul 5, 1994

US-PAT-NO: 5326707
DOCUMENT-IDENTIFIER: US 5326707 A

TITLE: Composition and device for urinary protein assay and method of using the same

DATE-ISSUED: July 5, 1994

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Franke; Gunter	Leichlingen			DE
Salvati; Michael	St. Paul	MN		
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US-CL-CURRENT: 436/86; 252/408.1, 422/56, 436/87, 436/88

CLAIMS:

What is claimed is:

1. An indicator reagent composition capable of exhibiting a sufficient color transition upon contacting a protein-containing test sample to demonstrate the presence or concentration of protein in the test sample consisting essentially of:

(a) an indicator dye capable of interacting with a protein and exhibiting a color transition upon such interaction, said indicator dye being present in an amount of about 0.05 to about 0.6 millimoles per liter of the composition and wherein the indicator dye is selected from the group consisting of 3',3",5,5"-tetraiodo-3,4,5,6-tetrabromophenolsulfophthalein, 3,3"-diiodo-5,5",3,4,5,6-hexabromophenolsulfophthalein, and combinations thereof;

(b) a buffer present in an amount of about 250 to about 750 millimoles per liter of the composition wherein the buffer is selected from the group consisting of citric acid, maleic acid, tartaric acid, phthalic acid, sulfosalicyclic acid, succinic acid, malonic acid, their respective alkali metal and ammonium salts and combinations thereof;

(c) a hydrophobic polymeric compound present in an amount of about 1% to about 8% by weight per milliliter of the composition having the general structural formula:

H--[--A--R.sub.1 --].sub.n --A--E,

wherein A is ##STR18## and PO is an oxypropylene unit, EO is an oxyethylene unit, y is a number in the range of 0 to about 20, z is a number in the range

of 0 to about 20, the sum of y+z is a number in the range of about 2 to about 20, and R.sub.2 and R.sub.3 are selected, independently, from the group consisting of hydrogen, alkyl group, an aralkyl group, and an aryl group;

R.sub.1 is methylene or oxygen;

n is a number in the range of 1 to about 8; and

E is hydrogen or methylol when R.sub.1 is methylene, or E is hydroxy when R.sub.1 is oxygen; and

(d) a carrier vehicle for said composition.

2. The composition of claim 1 wherein the buffer buffers the composition at a pH of 2 to 4.

3. The composition of claim 1 wherein the hydrophobic polymeric compound is present in the amount of about 2% to about 6%, by weight, per milliliter of the composition.

4. The composition of claim 1 wherein the hydrophobic polymeric compound has a molecular weight in the range of about 800 to about 12,000.

5. The composition of claim 1 wherein the substituents R.sub.2 and R.sub.3 of the hydrophobic polymeric compound are selected, independently, from the group consisting of hydrogen, an alkyl group including from one to about 22 carbon atoms, .alpha.-methylstyryl, and phenyl.

6. The composition of claim 1 wherein the moiety --A--R.sub.1 --of the hydrophobic polymeric compound is ##STR19## wherein R.sub.2 ' and R.sub.3 ' are, independently, hydrogen or an alkyl group including one to about 22 carbon atoms.

7. The composition of claim 1 wherein n is a number in the range of about 2 to about 5.

8. The composition of claim 1 wherein the moiety --A--R.sub.1 --of the hydrophobic polymeric compound is ##STR20## wherein PO is an oxypropylene unit, EO is an oxyethylene unit, y' and z' are, independently, numbers in the range of about 2 to about 8, the sum y'+z' is a number in the range of about 6 to about 16; and R.sub.2 ' is an alkyl group including from about 6 to about 18 carbon atoms.

9. The composition of claim 8 wherein y' and z' are, independently, numbers in the range of about 5 to about 6; the sum y'+z' is a number in the range of about 10 to about 12; and R.sub.2 ' is an alkyl group including from about 7 to about 12 carbon atoms.

10. The composition of claim 1 having a buffered pH in the range of about 2 to about 4.

11. The method of contacting a test sample with an indicator reagent composition to determine the presence of concentration of protein in the test sample, said method being essentially free of interferences attributed to specific gravity, said method comprising the steps of:

(i) contacting the test sample with an indicator reagent composition consisting essentially of:

(a) an indicator dye capable of interacting with a protein and exhibiting a color transition upon such interaction, said indicator dye being present in an amount of about 0.05 to about 0.6 millimoles per liter of the composition and wherein the indicator dye is selected from the group consisting of 3',3",5,5"-tetraiodo-3,4,5,6-tetrabromophenolsulfophthalein, 3,3"-diiodo-5,5",3,4,5,6-hexabromophenolsulfophthalein, and combinations thereof;

(b) a buffer present in an amount of about 250 to about 750 millimoles per liter of the composition wherein the buffer is selected from the group consisting of citric acid, maleic acid, tartaric acid, phthalic acid, sulfosalicylic acid, succinic acid, malonic acid, their respective alkali metal and ammonium salts and combinations thereof;

(c) a hydrophobic polymeric compound present in an amount of about 1% to about 8% by weight per milliliter of the composition having the general structural formula:

H--[--A--R.sub.1 --].sub.n --A--E,

wherein A is ##STR21## and PO is an oxypropylene unit, EO is an oxyethylene unit, y is a number in the range of 0 to about 20, z is a number in the range of 0 to about 20, the sum of y+z is a number in the range of about 2 to about 20, and R.sub.2 and R.sub.3 are selected, independently, from the group consisting of hydrogen, alkyl group, an aralkyl group, and an aryl group;

R.sub.1 is methylene or oxygen;

n is a number in the range of 1 to about 8; and

E is hydrogen or methylol when R.sub.1 is methylene, or E is hydroxy when R.sub.1 is oxygen; and

(d) a carrier vehicle for said composition; and

(ii) determining the presence or concentration of protein in the test sample from a resulting intensity or degree of the color transition of the indicator reagent composition.

12. The method of claim 11 wherein the intensity and degree of the color transition is determined visually or by instrument.

13. The method of claim 11 wherein the presence or concentration of protein is determined by a dry phase assay.

14. The method of claim 11 wherein the test sample is a biological sample.

15. The method of claim 14 wherein the biological sample is urine, blood plasma or blood serum.

16. The method of claim 15 wherein the urine has a specific gravity of about 1.005 to about 1.030.

17. The method of claim 11 wherein the test sample includes from 0 mg/dL protein to about 30 mg/dL protein.

18. The method of claim 11 wherein the buffer buffers the indicator reagent composition at a pH of 2 to 4.

19. The method of claim 11 wherein the number n of the hydrophobic polymeric compound is in the range of about 2 to about 5.

20. The method of claim 11 wherein the moiety --A--R.sub.1 --of the hydrophobic polymeric compound is ##STR22## wherein R.sub.2 ' and R.sub.3 ' are, independently, hydrogen or an alkyl group including one to about 22 carbon atoms.

21. The method of claim 20 wherein n is a number in the range of about 2 to about 5.

22. The method of claim 11 wherein the moiety --A--R.sub.1 --of the hydrophobic polymeric compound is ##STR23## wherein PO is an oxypropylene unit, EO is an oxyethylene unit, y' and z' are, independently, numbers in the range of about 2 to about 8, the sum y'+z' is a number in the range of about 6 to about 16; and R.sub.2 ' is an alkyl group including from about 6 to about 18 carbon atoms.

23. The method of claim 22 wherein y' and z' are, independently, numbers in the range of about 5 to about 6; the sum y'+z' is a number in the range of about 10 to about 12; and R.sub.2 ' is an alkyl group including from about 7 to about 12 carbon atoms.

24. The method of claim 11 wherein the liquid test sample is urine.

25. The method of claim 11 wherein the liquid test sample contains about 30 mg/dL or less of protein.

26. The method of claim 11 wherein the liquid test sample contains about 15 mg/dL or less of protein.

27. The method of claim 11 wherein the liquid test sample is urine having a specific gravity of about 1.005 to about 1.030.

28. An analyte detection device for contacting with a liquid test sample to determine the presence or concentration of protein in the liquid test sample, comprising:

(i) a support strip; and

(ii) a test pad comprising a carrier matrix having an indicator reagent composition incorporated therein, said indicator reagent composition consisting essentially of:

(a) an indicator dye capable of interacting with a protein and exhibiting a color transition upon such interaction, said indicator dye being present in an amount of about 0.05 to about 0.6 millimoles per liter of the composition and wherein the indicator dye is selected from the group consisting of 3',3",5,5"-tetraiodo-3,4,5,6-tetrabromophenolsulfophthalein, 3,3"-diiodo-5,5",3,4,5,6-

hexabromophenolsulfophthalein, and combinations thereof;

(b) a buffer in an amount of about 250 to about 750 millimoles per liter of the composition wherein the buffer is selected from the group consisting of citric acid, maleic acid, tartaric acid, phthalic acid, sulfosalicyclic acid, succinic acid, malonic acid, their respective alkali metal and ammonium salts and combinations thereof;

(c) a hydrophobic polymeric compound present in an amount of about 1% to about 8% by weight per milliliter of the composition having the general structural formula:

H--[--A--R.sub.1 --].sub.n --A--E,

wherein A is ##STR24## and PO is an oxypropylene unit, EO is an oxyethylene unit, y is a number in the range of 0 to about 20, z is a number in the range of 0 to about 20, the sum of y+z is a number in the range of about 2 to about 20, and R.sub.2 and R.sub.3 are selected, independently, from the group consisting of hydrogen, alkyl group, an aralkyl group, and an aryl group;

R.sub.1 is methylene or oxygen;

n is a number in the range of 1 to about 8; and

E is hydrogen or methylol when R.sub.1 is methylene, or E is hydroxy when R.sub.1 is oxygen; and

(d) a carrier vehicle for said composition.

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L4: Entry 10 of 10 File: USPT Mar 2, 1999

US-PAT-NO: 5876969
DOCUMENT-IDENTIFIER: US 5876969 A

TITLE: Fusion polypeptides comprising human serum albumin, nucleic acids encoding same, and recombinant expression thereof

DATE-ISSUED: March 2, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Fleer; Reinhard	91440 Bures-sur-Yvette			FR
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US-CL-CURRENT: 435/69.7; 435/252.3, 435/320.1, 435/325, 514/12, 530/350, 530/362, 536/23.4, 536/24.1

CLAIMS:

We claim:

1. A fusion polypeptide comprising human serum albumin or a natural variant thereof and a separate, heterologous therapeutically active polypeptide attached to each of the C-terminal end and the N-terminal end of said human serum albumin.

2. A fusion polypeptide according to claim 1, wherein said therapeutically active polypeptide is of human origin.

3. A fusion protein according to claim 2, wherein the polypeptide attached to said C-terminal end of said albumin has the same chemical composition as that of the polypeptide attached to said N-terminal end of said albumin.

4. A fusion polypeptide according to claim 1, wherein said therapeutically active polypeptide comprises all or part of a polypeptide selected from the group consisting of enzymes, enzyme inhibitors, antigens, antibodies, hormones, coagulation factors, interferons, cytokines, growth factors, differentiation factors, factors involved in the genesis of bone tissues, factors involved in the resorption of bone factors, chemotactic factors, cell motility factors, migration factors, cytostatic factors, bactericidal factors, antifungal factors, plasma adhesive molecules, interstitial adhesive molecules and extracellular matrices.

5. A nucleotide sequence encoding a fusion polypeptide according to claim 1.

6. A nucleotide sequence according to claim 5, further comprising a leader sequence permitting the secretion of the expressed polypeptide.

7. An expression cassette comprising a nucleotide sequence according to claim 5 under the control of a promoter region.

8. A self-replicating vector comprising an expression cassette according to claim 7.

9. An expression cassette according to claim 7, further comprising a region for the termination of transcription.

10. A recombinant cell comprising a nucleotide sequence according to claim 5.

11. A recombinant cell according to claim 10, which is a yeast, an animal cell, a fungus or a bacterium.

12. A recombinant cell according to claim 11, which is a yeast.

13. A recombinant cell according to claim 12, which is a yeast of the genus Saccharomyces or Kluyveromyces.

14. A process for preparing a fusion polypeptide comprising a therapeutically active polypeptide fused to each of the C-terminal end and N-terminal end of human serum albumin or to a natural variant thereof, comprising culturing a recombinant cell of claim 10 under conditions for expression, and recovering the polypeptide produced.

15. A composition comprising a fusion polypeptide according to claim 1 and a pharmaceutically acceptable carrier.

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L2: Entry 2 of 2 File: USPT May 22, 2001

US-PAT-NO: 6235489
DOCUMENT-IDENTIFIER: US 6235489 B1

TITLE: Method for diagnosing and distinguishing stroke and diagnostic devices for use therein

DATE-ISSUED: May 22, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Jackowski; George	Kettleby			CA

US-CL-CURRENT: 435/7.92; 422/55, 422/56, 422/58, 422/60, 422/61, 424/9.1, 435/13, 435/4, 435/5, 435/6, 435/7.1, 435/7.21 , 435/7.4, 435/7.9, 435/7.94, 435/7.95, 435/9, 435/969, 435/970, 435/973, 435/975, 436/161, 436/164, 436/514, 436/528, 436/530, 436/531, 436/807, 436/808, 436/810, 436/811

CLAIMS:

What is claimed is:

1. A method for confirming the occurrence of a hemorrhagic cerebral event or an ischemic cerebral event and distinguishing the type of event which has occurred comprising:

a. analyzing a body fluid of a patient to detect the presence and concentration of four markers of cerebral events wherein

i. a first marker is myelin basic protein,

ii. a second marker is the beta isoform of S100 protein,

iii. a third marker is neuronal specific enolase,

iv. a fourth marker is a brain endothelial cell membrane protein, and

b. comparing said four markers to specific threshold values of each of the markers to determine the presence of statistically significant concentrations thereof of at least about two standard deviations above normal levels;

wherein said step of comparing said four markers confirms the occurrence of an ischemic cerebral event or a hemorrhagic cerebral event and further distinguishes which type of cerebral event has occurred.

2. A method as defined in claim 1 wherein said body fluid is selected from the group consisting of blood, blood components and cerebrospinal fluid.

3. A method as defined in claim 1 wherein each of said analyses is carried out on a single sample of body fluid.

4. A method as defined in claim 1 wherein at least one of said analyses is carried out on a first sample of body fluid and at least another of said analyses is carried out on a second sample of body fluid.

5. A method as defined in claim 4 wherein said first and said second samples of body fluid are taken at different time periods.

6. A method as defined in claim 1 wherein said brain endothelial cell membrane protein is selected from one or more of the group consisting of Thrombomodulin, Glucose Transporter I in the dimeric or tetrameric form, Neurothelin, Gamma Glutamyl Transpeptidase, and P-glycoprotein.

7. A method as defined in claim 1 wherein at least one of said analyses comprises contacting said body fluid with an antibody which is specific for said marker.

8. A method as defined in claim 7 wherein at least one of said analyses is carried out with an enzyme-labeled immunoassay method.

9. A method as defined in claim 1 and further including the step of analyzing said body fluid for a fifth marker protein, wherein said fifth marker protein is cell type specific with respect to one of said first, second or third markers and has a correspondingly higher molecular weight than said first, second or third marker.

10. A method as defined in claim 9 wherein at least one of said analyses comprises contacting said body fluid with an antibody which is specific for said marker.

11. A method as defined in claim 10 wherein at least one of said analyses is carried out with an enzyme-labeled immunoassay method.

12. A method as defined in claim 1 and further including the step of analyzing a second sample of a body fluid from said patient for said four markers, said second sample of body fluid being taken at a time subsequent to the time at which said body fluid analyzed in step a is taken.

13. A diagnostic kit for confirming the occurrence of a hemorrhagic cerebral event or an ischemic cerebral event and distinguishing the type of event which has occurred comprising at least four antibodies which are specific for each of four different marker proteins, said antibodies immobilized on a solid support, wherein

a. a first marker protein is myelin basic protein and a first antibody is specific therefor,

b. a second marker protein is the beta isoform of S100 protein and a second antibody is specific therefor,

c. a third marker protein is neuronal specific enolase and a third antibody is specific therefor,

d. a fourth marker protein is a brain endothelial cell membrane protein and a fourth antibody is specific therefor and at least four labeled antibodies, each of said labeled antibodies binding to one of said marker proteins, and

e. means for comparing said four markers to specific threshold values of each of the markers to determine the presence of statistically significant concentrations thereof of at least about two standard deviations above normal levels;

wherein said step of comparing said four markers confirms the occurrence of an ischemic cerebral event or a hemorrhagic cerebral event and further distinguishes which type of cerebral event has occurred.

14. A diagnostic kit as defined in claim 13 wherein each of said four antibodies are immobilized on the same solid support.

15. A diagnostic kit as defined in claim 13 wherein at least one of said four antibodies is immobilized on a first solid support and at least another of said four antibodies is immobilized on a second solid support.

16. A diagnostic kit as defined in claim 13 wherein at least one of said labeled antibodies comprises an enzyme-labeled antibody.

17. A diagnostic kit as defined in claim 13 wherein said brain endothelial cell marker protein is selected from one or more of the group consisting of Thrombomodulin, Glucose Transporter I in the dimeric or tetrameric form, Neurothelin, Gamma Glutamyl Transpeptidase, and P-glycoprotein.

18. A diagnostic kit as defined in claim 13 and further including a fifth antibody which is specific for a fifth marker protein, wherein said fifth marker protein is cell type specific with respect to one of said first, second or third markers and has a correspondingly higher molecular weight than said first, second or third marker, and a fifth labeled antibody which binds to said fifth marker protein.

19. A diagnostic kit as defined in claim 18 wherein said fifth labeled antibody comprises an enzyme-labeled antibody.

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L1: Entry 1 of 1 File: USPT Aug 14, 2001

US-PAT-NO: 6274305
DOCUMENT-IDENTIFIER: US 6274305 B1

TITLE: Inhibiting proliferation of cancer cells

DATE-ISSUED: August 14, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Sonnenschein; Carlos	Boston	MA		
Soto; Ana M.	Boston	MA		

US-CL-CURRENT: 435/4; 435/388, 435/405, 435/406, 435/407

CLAIMS:

What is claimed is:

1. A method of measuring human cancer cell proliferation, comprising:

a) providing:

i) a human cancer patient,

ii) an albumin-derived peptide, wherein said albumin-derived peptide is truncated in length, thereby shorter than the 585 amino acid long human serum albumin, and comprises domains I and II of human serum albumin;

b) obtaining cancer cells from said patient;

c) culturing said cancer cells in serum-free media;

d) contacting said cells ex vivo with said albumin-derived peptide; and

e) measuring the extent of cancer cell proliferation.

2. The method of claim 1, wherein said cancer cells are obtained from a biopsy.

3. The method of claim 1, wherein said cancer cells are selected from the group consisting of breast cancer cells and prostate cancer cells.

4. The method of claim 1, wherein said albumin-derived peptide consists of the amino acids 1-387 of human serum albumin.

5. The method of claim 1, wherein said albumin-derived peptide consists of the amino acids 1-388 of human serum albumin.

6. A method of measuring human cancer cell proliferation, comprising:

a) providing:

i) a human cancer patient,

ii) an albumin-derived peptide, wherein said albumin-derived peptide is truncated, thereby shorter in length than the 585 amino acid long human serum albumin, and comprises domains I and II of human serum albumin; and

iii) one or more hormones or hormone analogues;

b) obtaining cancer cells from said patient;

c) culturing said cells in serum-free culture media in the presence of said albumin-derived peptide and said one or more hormones or hormone analogues; and

d) measuring cancer cell proliferation.

7. The method of claim 6, wherein said cancer cells are obtained from a biopsy.

8. A The method of claim 6, wherein said cancer cells are selected from the group consisting of breast cancer cells and prostate cancer cells.

9. The method of claim 6, wherein said hormone comprises an estrogen.

10. The method of claim 6, wherein said albumin-derived peptide consists of domains I and II of human serum albumin.

11. The method of claim 6, wherein said albumin-derived peptide consists of the amino acids 1-387 of human serum albumin.

12. The method of claim 6, wherein said albumin-derived peptide consists of the amino acids 1-388 of human serum albumin.

13. A method of measuring human cancer cell proliferation, comprising:

a) providing:

i) a human cancer patient,

ii) an albumin-derived peptide, said peptide consisting of the N-terminal region of the 585 amino acid sequence of human serum albumin, said N-terminal region having the same amino acid sequence as said human serum albumin up to and including a terminal amino acid selected from the group consisting of amino acids 360-430 of said human serum albumin;

b) obtaining cancer cells from said patient;

c) culturing said cancer cells in serum-free media;

d) contacting said cells ex vivo with said albumin-derived peptide; and

e) measuring the extent of cancer cell proliferation.

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